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STUDIES IN THE RESPIRATORY EXCHANGE OF INFANTS *

FRANCIS G. BENEDICT AND FRITZ B. TALBOT

BOSTON

An extensive study of the gaseous exchange of infants has been in progress for three years in connection with the Nutrition Laboratory and with the Massachusetts General Hospital. Pending the development of a method for determining the oxygen consumption directly — a factor that we deemed of very great importance — a preliminary communication was made in this journal[1] in 1912. Since the appearance of this article, the apparatus and technic have been perfected so as to include direct determinations of the oxygen consumption. An apparatus has been constructed, tested and installed in a special room in the Massachusetts General Hospital, and except during the summer months, studies of the gaseous metabolism of infants have been made daily since January, 1913. Although the investigation is still in progress, sufficient data have been accumulated to justify the presentation of material *in extenso* in a publication of the Carnegie Institution of Washington.[2] A full description of the apparatus and technic, the clinical history of the infants studied and the statistical data for each observation are given in that publication for permanent record. It is our purpose in this communication to present first, a complete collection of the literature bearing on this subject up to the present date, and second, an amplification of our data by a new series of observations and finally an abstract of our results.

PREVIOUS OBSERVATIONS ON THE GASEOUS METABOLISM OF INFANTS

The earliest record that we have been able to find of the measurement of the gaseous metabolism of an infant is that reported by J. Forster of Munich, in 1877.† In an effort to explain the well-known

* Submitted for publication, May 8, 1914.

* From the Nutrition Laboratory of the Carnegie Institution of Washington and the Children's Department of the Massachusetts General Hospital, Boston, Mass.

1. Benedict and Talbot: Some Fundamental Principles in Studying Infant Metabolism, AM. JOUR. DIS. CHILD., 1912, iv, 129.

2. Benedict and Talbot: The Gaseous Metabolism of Infants with Special Reference to Its Relation to Pulse-Rate and Muscular Activity, Carnegie Institution of Washington, Publication 201, 1914.

† Forster: Amtl. Ber. d. 50. Versamml. deutsch. Naturf. u. Aerzte in München, Munich, 1877, p. 355.

fact that children consume a larger amount of food in proportion to their body-weight than do adults, this investigator made determinations of the carbon dioxid excretion in fourteen experiments on children varying in age from 14 days to 9 years. His results all showed that 10 or 12 gm. of carbon dioxid were given off per hour for every 10 kg. of body-weight. With adults on the same basis, the carbon dioxid given off under conditions of rest and approximate hunger was 4 to 5 gm. per hour; with an average diet, 5 to 6 gm.; and with food and work, 7 gm. The author points out that the youthful organism, even in the condition of hunger, produces per unit of weight at least twice the amount of carbon dioxid which is produced by the adult body. The fact is also recognized that the infant can develop a considerable amount of work.

The experiments were made with the large Pettenkofer-Voit respiration chamber in Munich, but the protocols were never published, and aside from the statement that the children were at rest, no further details are given as to the muscular activity or the pulse-rate.

In 1885 Richet,[3] in describing his calorimeter, states that he has two chambers, one of which, having a capacity of about 1,500 liters of air, is used for experiments with infants. He cites an experiment with an infant of 9 kg., who was in the chamber for one hour and ten minutes, and gives protocols for another experiment, one hour in length, presumably with the same infant. In summing up his averages he refers to numerous experiments on infants weighing from 6 to 9 kg., and includes observations made with environmental temperatures ranging from 18 C. to 25 C. He concludes that the infant produces on the average 4 calories per kilogram of body-weight per hour. Richet discusses especially the relationship between the body-surface and the heat-production.

Two years later, Langlois[4] conducted experiments on children with Richet's calorimeter, in which only the heat-production was measured. From 17 controlled experiments, all with infants weighing about 7 kg., Langlois concludes that the heat-production is increased as the environmental temperature is lowered. As a result of a study of the influence of the time of day on the heat-production, he also concludes that there are two maximum values at approximately 11 a. m. and 3 p. m., corresponding to the values for the absorption of oxygen found by Fredericq.[5]

Langlois' discussion of the relationships between the heat-production and the body-weight and the heat-production and the body-surface

3. Richet: Archiv. de physiol. norm. et. path., 1885, Series 3, xv, 237.
4. Langlois: Centralbl. f. Physiol., 1887, i, 237.
5. Fredericq: Arch. de Biol., 1882, iii, 731.

is of special interest in connection with our research. As will be seen from his figures given in Table 1, the smaller the child the larger was the heat-production per kilogram of body-weight. The author points out, however, that if the heat-production and body-surface are compared, as is done in Table 2, the uniformity is remarkable. He gives a very unsatisfactory explanation of his unit of surface, but brings out the fundamental idea that the heat per unit of body-surface is essentially the same for an infant as for an adult weighing 65 kg., namely, 14 to 17 calories. No information is given regarding the muscular activity, the age, or the pulse-rate of these infants.

In another paper, Langlois[6] refers to Richet's observations on normal children weighing from 7 to 10 kg. with a heat-production of approximately 4,000 calories per kilogram per hour, and reports his own results with sick infants in which he finds a direct relationship

TABLE 1.—Relationship Between Heat-Production and Body-Weight of Infants (Langlois)

Body-Weight (kg.)	Heat-Production per kg. of Body-Weight (cals.)
Two children 1.8	6.40
Child 2.5	4.80
Children from.....3.0 to 4.0	4.20
Children from.....7.0 to 8.0	4.12
Children from.....9.0 to 10.0	3.93

between body-temperature and heat-production. Infants having temperatures below 37.5 C., which he takes as normal, had a heat-production less than 4 calories per kilogram of body-weight per hour, while those with temperatures above 37.5 C. had a higher heat-production; thus, with a body-temperature of 35.5 C., the heat-production was equal to 2,900 calories, while with a body-temperature of 40.5 C., it was equal to 4,600 calories.

Langlois' calorimeter was subsequently used by Variot and Saint-Albin[7] in studying the calorimetry of atrophic infants. The tests of this calorimeter published by Saint-Albin[8] show a possible error of plus or minus 10 per cent., thus indicating that the apparatus can hardly be

6. Langlois: Compt. rend de l'Acad. des Sci. de l'Institut de France, 1887, civ, 860.

7. Variot and Saint-Albin: Bull. Soc. de pédiat., 1903, v, 246 and 307. See, also, an extensive discussion of these researches in the thesis by Saint-Albin: Etude sur la calorimétrie des infants atrophiques, Paris, 1904, No. 295.

8. Saint-Albin: Etude sur la calorimétrie (Note 7), p. 25.

considered an instrument of precision. As Saint-Albin points out himself, his check tests differ considerably from those of Langlois.

Variot and Saint-Albin studied a large number of atrophic infants. Their conclusions, reported by Saint-Albin, are especially interesting in connection with this report of our researches, since they show that (using their terminology) out of 33 atrophic infants, there were 11 *"hyperrayonnants,"* 16 *"hyporayonnants"* and 6 *"rayonnants normalement."*[9]

Of the numerous forms of calorimeters reported to the French scientific societies by d'Arsonval, one[10] was employed by Bonniot[11] in 1898 for a study of the heat-production of infants with temperature disturbances, but he found no regular relationship between heat radiation and rectal temperature. A detailed presentation of Bonniot's results may be found in his thesis.[12]

TABLE 2.—RELATIONSHIP BETWEEN HEAT PRODUCTION AND BODY-SURFACE OF INFANTS (LANGLOIS)

Body-Weight kg.	Body-Surface	Heat-Production		
		Per kg. of Body-Weight Cals.	Per Unit of Surface cals.	Per Sq. Meter of Body-Surface† cals.
10	9.142*	3.920	17	1,690
9	2.106	3.900	16	1,620
7	1.778	4.120	16	1,580
6	1.638	4.200	15	1,500
4	1.135	4.300	15	1,370
2	0.780	6.000	15	1,510

*This figure is quoted from Langlois and as his discussion of body-surface is very confusing, it is impossible to make a correction, which is obviously much needed.

†As calculated by Camerer using Meeh's formula (Camerer: Der Stoffwechsels des Kindes, Tübingen, 1896, p. 109).

The most recent contribution from French laboratories on direct calorimetry with which we are familiar is that of Variot and Lavialle[13] in 1912. In this interesting communication, in which the fundamental principles of infant calorimetry are well considered, the authors state

9. Saint-Albin: Etude sur la calorimétrie (Note 7), p. 39.

10. See note on this particular calorimeter by d'Arsonval: Mem. Soc. de biol., 1898, p. 248.

11. Bonniot: Mém. Soc. de biol., 1898, p. 249. For a critique of the Richet and d'Arsonval calorimeters, see Bonniot: Calorimétrie infantile ètat de la question, Clinique Infantile, 1906, iv, 289.

12. Bonniot: De l'hyperthermie dans la fièvre; essai de calorimétrie clinique, Paris, 1900, No. 419.

that they used the modified form of the d'Arsonval calorimeter which was calibrated by electrical resistance. The gaseous metabolism was not studied and no statement was made as to the muscular activity of the infants. The authors conclude that the heat-output of infants increases in proportion as the weight decreases and lay great emphasis on the effect of clothing on radiation. They likewise believe that the supply of adipose tissue may materially modify the radiation.

Mensi[14] of Turin, without stating the apparatus employed or even the fundamental principle, reports a series of observations on five newborn infants varying in age from 6 hours and 5 minutes to 7 days, 17 hours and 54 minutes. In these experiments the oxygen consumption was determined as well as the carbon dioxid production. The results are given in Table 3. The statement is made that the infants were quiet in each case, but no pulse records are given.

A very interesting series of experiments on infants was carried out by Scherer in the institute of Professor Marês in Prague[15] with an apparatus on the Regnault-Reiset principle, the oxygen being supplied from a bomb. The author states that the infants found themselves in "complete physiological condition" inside the chamber. In this series, fifty-five experiments were made in the spring and summer and thirty experiments in the winter, each one being about two hours long. No information is given regarding the activity of the infants or the pulse-rate. The fact that the average respiratory quotients were considerably below 0.6 points strongly to an error in the method. The author concludes that the intensity of the respiratory exchange is dependent on the body-weight and is inversely proportional to it.

Two years later the classic monograph of Rubner and Heubner[16] appeared. In discussing the earlier observations of Forster, they add the significant fact that Forster's experimental periods were but one hour long. As their own work was done with the Pettenkofer chamber, they criticize adversely the closed circuit apparatus used by Scherer, and particularly the fundamental principle of using experiments with short periods, their paper setting forth fully the arguments in favor of the long experimental period and the Pettenkofer type of respiration chamber as compared with the short period and the Regnault-Reiset chamber. The Pettenkofer chamber, which had pre-

13. Variot and Lavialle: Bull. and mém. Soc. méd. d. hôp. de Paris, 1912, Series 3, xxxiii, 410. See, also, Clinique Infantile, 1912, x, 229, and Report of the Congrés National des Gouttes de Lait tenu à Fécamp les 26, 27, et 28 Mai, 1912, p. 79.

14. Mensi: Gior. d. r. Accad. di med. di Torino, 1894, lvii, 301.

15. Scherer: Jahrb. f. Kinderh., 1896, new series, xliii, 471.

16. Rubner and Heubner: Ztschr. f. Biol., 1898, xxxvi, 1.

TABLE 3.—Summary of Experiments on Respiratory Exchange of New-Born Infants (Mensi)

Age d., h., m.	Sex	Body-Weight kg.	Length of Experiment minutes	Oxygen Consumed			Carbon Dioxid Produced				Respiratory Quotient
				Total c.c.	Per Minute c.c.	Per Kg. per Min. c.c.	Total c.c.	Per Min. c.c.	Per Kg. per Minute		
									c.c.	mg.	
6 5	M.	2.70	173	5,707	32.9	12.18	4,174	24.1	8.92	16.08	0.73
1 2 47	M.	3.00	173	6,470	37.4	12.46	3,844	22.2	7.40	13.34	0.593
3 1 55	M.	2.92	159	6,216	39.09	13.38	3,442	21.64	7.41	13.36	0.55
3 7 22	F.	2.47	171	5,463	31.9	12.91	3,586	20.9	8.46	15.25	0.655
7 17 54	M.	2.32	149	4,997	33.5	14.43	2,979	19.9	8.57	15.45	0.59

viously been described,[17] was slightly modified for the studies of Rubner and Heubner, a small chamber being used.

The fundamental question studied by Rubner and Heubner was the nourishment of an infant from a practical point of view; and they were accordingly more interested in the average daily requirement of an infant for nourishment than in the physiologic fact of the minimum requirement for comparison with other individuals. The subject — a "normal" infant — was 9 weeks old at the time of the observation and weighed 5,220 gm. The infant was placed in the respiration chamber and removed and fed from six to eight times each day, the time thus lost being carefully recorded. Ocular observations of the muscular activity were made and a general impression for each day recorded. For much of the time, the infant was awake but not crying. On the basis of twenty-four hours the authors found a difference of 22 per cent. between the minimum and maximum carbon dioxid production. They state that this difference is due to the unequal activity of the infant, emphasizing especially the fact that disturbance of sleep during the night influences the total daily average of the metabolism.

Using the formula of Meeh[18] and a body-weight of 5.1 kg., they compute the body-surface to be equal to 3,500 square centimeters and find a carbon dioxid production of 13.5 gm. per square meter of body-surface per hour. Comparing this value with those values found with adults, they state that the infant excreted less carbon dioxid per square meter of body-surface than did the adults, and explain this by the fact that the infant was asleep a part of the time while the determinations with adults were made only when the subjects were awake. Having pointed out that their results contradict those of Sondén and Tigerstedt,[19] which showed an increased production of carbon dioxid in youth, they emphasize the fact that the carbon dioxid is essentially proportional to the body-surface with human individuals of any size.

Shortly after the publication of their investigations with a normal, breast-fed infant, Rubner and Heubner[20] reported a comparative study with a normal and an atrophic infant, neither being breast-fed. This study was carried out on the same plan as that used for the former experiment. The "normal" infant weighed 7.57 kg., was 7½ months old and appeared to be in good health. She was fed on milk and milk-sugar and throughout the observation was said to be in general *recht ruhig*. The results were compared with those obtained with the breast-fed infant in the previous experiment, the hourly excretion of carbon

17. Wolpert: Arch. f. Hyg., 1896, xxvi, 32.

18. Meeh uses the formula $S = 11.9 \sqrt[3]{w^2}$. (Ztschr. f. Biol., 1879, xv, 425.)

19. Sondén and Tigerstedt: Skandin. Arch. f. Physiol., 1895, vi, 1.

20. Rubner and Heubner: Ztschr. f. Biol., 1899, xxxviii, 315.

dioxid per square meter of body-surface being but 13.5 gm. for the breast-fed infant, which weighed but 5 kg., and 17.3 gm. for the artificially fed infant, which weighed 7.6 kg.

The second portion of the paper deals with the metabolism of the atrophic infant, artificially fed with cow's milk and *"Kindermehl."* Their results are given in Table 4. The authors conclude that there was nothing abnormal in the metabolism of the atrophic infant.

The first extensive study exclusively with atrophic infants was made by Poppi.[21] A respiration apparatus of the closed-circuit type was probably used, as both the carbon dioxid production and the oxygen consumption were measured, though little is said of the method. An abstract of the results obtained with seven infants is given in Table 5. The respiratory quotients all seem unusually high, and this fact throws doubt on the accuracy of the research. It is probable,

TABLE 4.—RESULTS OF EXPERIMENTS WITH A NORMAL INFANT AND AN ATROPHIC INFANT. (RUBNER AND HEUBNER)

Description of Subject	Food	Period	Calories per Square Meter of Body-Surface
Normal.....	Breast-fed	...	1,006
	Cow's milk.....	I	1,143
	Cow's milk.....	II	1,233
	Cow's milk.....	III	1,378
Atrophic.....	Cow's milk.....	I	1,090
	Cow's milk.....	II	1,171
	Meal	...	1,036

however, that the carbon dioxid determinations are well within the limits of accuracy, as is usual with methods of this type. From the protocols of one of Poppi's studies, it appears that the experiments were each two hours long, but no estimations are given regarding the muscular activity or the pulse-rate.

In 1904 Rubner and Heubner[22] reported another series of experiments covering a period of five days. The subject was a breast-fed infant, 5½ months old and weighing 9.7 kg. Notwithstanding the apparently large changes in the activity from day to day, the investigators found that the carbon dioxid output on the last four days was fairly constant — a fact which puzzled the authors, who suggest a compensatory influence in the life of the infant. They compare the results found in this observation with those secured with other infants

21. Poppi: Il ricambio materiale e il ricambio respiratorio nell'atrofia infantile, Bologna, 1900.

22. Rubner and Heubner: Ztschr. f. exper. Path. u. Therap., 1904-05, i, 1.

TABLE 5.—Results of Experiments on the Respiratory Exchange of Atrophic Infants (Poppi)

Name	Date 1899	Duration hrs.,min.	Body-Weight kg.	Age mos.	Carbon Dioxid Produced			Oxygen Consumed			Respiratory Quotient
					Total c.c.	Per 24 Hours liters	Per Kg. per Min c.c.	Total c.c.	Per 24 Hours liters	Per Kg. per Min c.c.	
P. L.....	July 11	1 15	3.425	9	2,166	40.62	8.237	2,084	40.02	8.114	1.015
N. B.....	July 20	2 00	3.865	10	3,900	46.80	8.409	3,820	45.84	8.236	1.021
C. F.....	Nov. 10	2 00	5.500	16	4,125	49.50	6.25	4,621	55.452	7.002	0.893
A. F.....	Nov. 12	2 00	3.465	7	3,177	38.13	7.642	3,027	36.324	7.280	1.050
M. G.....	Nov. 15	2 00	5.450	12	4,071	48.852	6.225	4,186	50.232	6.40	0.973
F. G.....	Dec. 8 1900	2 00	2.780	3½	2,667	32.004	8.07	2,642	31.704	7.92	1.019
E. N.....	Feb. 3	2 00	3.940	4	3,009	36.108	6.364	3,223	38.676	6.818	0.933

in the previous work done by them, and find an increase in the carbon dioxid output of 21 per cent. over the results obtained with the breast-fed infant previously studied. (See Table 6.) This increase they explain by saying that it is due to the greater activity of the infant in the last experiment.

TABLE 6.—METABOLISM OF INFANTS COMPARED (RUBNER AND HEUBNER)

Subjects and Diet	Body-Weight, kg.	Calories per Square Meter of Body-Surface per Day
Atrophic child (cow's milk)	3	1,090
Breast child	5	1,006
Child (cow's milk)	8	1,143
Child (breast, of this experiment)	10	1,219

In 1908 a report appeared of the first in a remarkable series of experiments carried out by Schlossmann and Murschhauser in Düsseldorf.[23] The protocols of this experiment were given in connection with a description of the testing of the modified Regnault-Reiset apparatus constructed by Zuntz and Oppenheimer. The authors, Schlossmann, Oppenheimer and Murschhauser, emphasize the importance of observa-

TABLE 7.—METABOLISM OF AN INFANT (SCHLOSSMANN AND MURSCHHAUSER) (PER SQUARE METER OF BODY-SURFACE PER HOUR)

	Oxygen Consumption, gm.	Carbon-Dioxid Production, gm.
Average during eight hours' sleep	11.0	13.78
Shortly after feeding	11.88	15.52
Three hours after feeding	10.42	12.68
Waking and sleeping	12.85	15.75

tions when the infant is asleep; they accordingly preferred to make their observations the first half of the night, feeding the infant with a large amount of breast-milk in the early evening. The measurements of the metabolism of the infant during this experiment are given in Table 7. During the experimental period the infant weighed 5.79 kg., the calculated body-surface[24] being 0.384 square meters.

23. Schlossmann, Oppenheimer and Murschhauser: Biochem. Ztschr., 1908, xiv, 385.

24. Surface $= 11.9 \sqrt[3]{w^2}$

The same infant was subsequently studied by Schlossmann and Murschhauser[25] at the ages of 144 days, 284 days and 380 days. They found no difference in the metabolism per square meter of body-surface and conclude that Rubner's law is correct and that the metabolic processes are proportional to the body-surface.

The report of the first extensive research made by Schlossmann and Murschhauser appeared in 1910.[26] This is of special interest, inasmuch as the authors recognize at the outset the importance of muscular repose and of determining the basal metabolism. Many valuable suggestions as to the selection of infants for such study are incorporated in the report. Observations were made on three female infants; the results of these are given in Table 8. The authors conclude that the carbon dioxid production and the oxygen consumption depend on the body-surface, being wholly independent of the age of

TABLE 8.—RESULTS OF FASTING EXPERIMENTS WITH INFANTS DURING APPROXIMATELY ABSOLUTE REST. (SCHLOSSMANN AND MURSCHHAUSER)

Subject	Age Days	Weight kg.	Body-Surface Square Meter	Carbon Dioxid per Square Meter per Hour, gm.	Oxygen per Square Meter per Hour gm.	Respiratory Quotient
S.....	174	5.010	0.3505	12.27	10.56	0.847
	180	5.115	0.3553	12.22	10.81	0.824
P.....	149	4.220	0.3124	12.35	10.52	0.856
	169	4.430	0.3228	12.64	11.08	0.832
L.....	87	4.980	0.3491	12.33	12.22	0.730
	93	5.040	0.3519	11.48	10.93	0.760

the subject, and draw the general conclusion that the infant produces per square meter of body-surface about 12 gm. of carbon dioxid and consumes about 11 gm. of oxygen per hour.

Recognizing the possibility that the environmental temperature may have an effect on the metabolism of the infant, Schlossmann and Murschhauser discussed this point in 1911,[27] giving the results of experiments with an infant in which the temperature of the surrounding atmosphere varied from 16.3 C. to 23.4 C. Another infant was studied with temperatures varying from 16.9 C. to 23.4 C. The results of this second experiment substantiated those obtained with the first infant, and the authors feel justified in concluding that the slight temperature changes found in experiments with an apparatus of the

25. Schlossmann and Murschhauser: Biochem. Ztschr., 1909, xviii, 499.
26. Schlossmann and Murschhauser: Biochem. Ztschr., 1910, xxvi, 14.
27. Schlossmann and Murschhauser: Biochem. Ztschr., 1911, xxxvii, 1.

Regnault-Reiset type are entirely without influence on the metabolism of the individuals studied.

The same investigators,[28] with a keen appreciation of the influence of muscular activity on metabolism, compared the results of observations with an infant who cried continuously for an hour with those obtained when the infant was approximately quiet. They estimated that the crying increased the carbon dioxid production 59.4 per cent. and the oxygen consumption 44 per cent.

In still another paper Schlossmann[29] discusses the general principles involved in the measurement of the respiratory exchange of infants and emphasizes the necessity of muscular repose and the absence of food, and the importance of measuring the basal metabolism. He again asserts that the heat per square meter of body-surface is constant and maintains that this is a proof that the metabolism of young individuals is not variable. In this paper, also, he discusses the amount of work the infant does, basing the discussion on results obtained in his experiments with crying infants. In many of his experiments Schlossmann measured the skin temperature of the infant by electrical methods and found that there was no increase in the temperature.

In a paper discussing his earlier experiments on infants of varying ages and particularly those with an atrophic infant, Schlossmann opposes the views defended by Kassowitz,[30] that the metabolism in smaller animals is more intense than in the large animals and that there is no relationship between the metabolism and the body-surface.[31] Schlossmann maintains that atrophic infants have a higher metabolism per unit of body-surface than normal infants, but that this points to the correctness of the Rubner law, since with these infants the relation between body-surface and body-weight is abnormal. As he made no measurements of the body-surface of these infants — a procedure that necessitated an enormous amount of work — no direct evidence is offered to show that there was an actual disproportion between the body-surface and the body weight.

In a paper which appeared after the publication of Schlossmann's criticism, Kassowitz[32] sums up his arguments against the belief that the metabolism is proportional to the body-surface, and using Schlossmann's own protocols, criticizes adversely the latter's deductions.

In a paper which has only recently appeared[33] Schlossmann again discusses the degree of activity and the amount of work done by

28. Schlossmann and Murschhauser: Biochem. Ztschr., 1911, xxxvii, 23.
29. Schlossmann: Deutsch. med. Wchnschr., 1911, xxxvii, 1633.
30. Kassowitz: Allgemeine Biologie, Vienna, 1904, iii, 221.
31. Schlossmann: Ztschr. f. Kinderh., 1912-13, v, 227.
32. Kassowitz: Ztschr. f. Kinderh., 1913, vi, 240.
33. Schlossmann: Monatschr. f. Kinderh., 1913, xii, 47. See also Am. Jour. Dis. Child., 1913, vi, 15.

infants in crying. He strongly emphasizes the necessity of noting the degree of repose during the observation, either by the ocular method used by himself or the graphic record devised in this laboratory. Unfortunately, at the time this paper was written, Schlossmann had not been able to compare the two methods.

Two later communications by Schlossmann and Murschhauser[34] on the metabolism of fasting infants have particular significance in connection with this report, as they discuss the ideal conditions for obtaining the basal metabolism.

Using a Pettenkofer-Voit respiration apparatus[35] in the Kaiserin Auguste Victoria-Haus in Charlottenburg, Birk and Edelstein[36] studied the respiratory exchange of a healthy, new-born infant weighing 3.2 kg. and having a length of 50 cm. The infant was completely wound in cotton wool so as to keep the body-temperature at a normal level. Although he was removed from the respiration chamber several times during the day, the infant remained in the apparatus for the greater part of the twenty-four hours. On the second day the carbon dioxid production per twenty-four hours was 55.6 gm., or 18.2 gm. per kilogram; on the third day the total amount was 47.59 gm., or 15.76 gm. per kilogram per twenty-four hours. The authors criticize the use of short experiments with a respiration apparatus by which the oxygen consumption can be determined and the respiratory quotients calculated, but express regret that with their method the oxygen consumption cannot be determined.

In a study made by Carpenter and Murlin[37] of the energy metabolism of pregnant women before and after the birth of the child, the energy metabolism of three new-born infants was also found per unit of weight and per unit of body-surface. The values were obtained by subtracting the measured metabolism of the mother from that of the mother and infant together.

The metabolism of an atrophic infant was studied by Niemann,[38] who used a Pettenkofer-Voit respiration apparatus in the children's clinic of the University of Berlin. The observation continued six days, the infant remaining in the chamber the greater part of each day. The measurements of the carbon dioxid production on the basis of twenty-four hours are given in Table 9. When these results are computed on the basis of carbon dioxid produced per square meter of body-surface,

34. Schlossmann and Murschhauser: Biochem. Ztschr., 1913, lvi, 355; ibid., 1914, lviii, 483.

35. Bahrdt and Edelstein: Jahrb. f. Kinderh., 1910, lxxii, 43.

36. Birk and Edelstein: Monatschr. f. Kinderh., 1910, ix, 505.

37. Carpenter, T. M., and Murlin, J. R.: The Energy Metabolism of Mother and Child Just Before and Just After Birth, Arch. Int. Med., 1911, vii, 184.

38. Niemann: Ztschr. f. Kinderh., 1913, vi, 375.

using the formula of Meeh and the constant 11.9, the author finds that this infant with an average body-weight during the six days of 3.28 kg. had a body-surface corresponding to 0.2626 square meter, and that the carbon dioxid excretion per square meter of body-surface was 18.5 gm. per hour.

TABLE 9.—RESULTS OF AN EXPERIMENT WITH AN ATROPHIC INFANT (NIEMANN)

Day	Carbon-Dioxid Production per Day gm.	Average Temperature of the Air, °C.
1	108.0	20.5
2	110.4	20.0
3	117.6	21.0
4	115.2	21.0
5	120.0	21.0
6	127.2	21.0
Maximum..	127.2	
Minimum..	108.0	
Average....	116.4	

The metabolism of another atrophic infant was studied in the Universitäts-Kinderklinik, Berlin, by Frank and Wolff.[39] Using the Pettenkofer-Voit respiration apparatus modified by Rubner, they made two series of experiments of four days each. The average values for carbon dioxid are given in Table 10. The authors especially comment

TABLE 10.—AVERAGE CARBON-DIOXID EXCRETION IN EXPERIMENTS WITH AN ATROPHIC INFANT (FRANK AND WOLFF)

	Period I	Period II
Total twenty-four hours.	127.61	148.81
Per hour	5.317	6.151
Per kilo per twenty-four hours	34.44	38.95
Per kilo per hour.....	1.435	1.623
Per square meter per hour	18.76	21.26

on the unusually high figures for the carbon dioxid excretion, and attempt to explain them by the disturbance between the computed body-surface and body-weight and the effect of a protein-rich diet, but expressly maintain that muscular activity played no rôle as the infant, except on the first day, was *sehr ruhig*.

39. Frank and Wolff: Jahrb. f. Kinderh., 1913, lxxviii, 1.

Bahrdt and Edelstein[40] also report an experiment with an atrophic infant, in which they used the respiration apparatus in Langstein's laboratory in the Kaiserin Auguste Victoria-Haus. The observation was made in three periods of four days each. In the first and last periods, the infant remained inside the chamber for the greater part of the twenty-four hours, being removed periodically, as is customary in experiments with this type of apparatus. Their final conclusion was that the heat-production of atrophic infants can be abnormally high aside from any effect which the environmental temperature or the body activity may have on it.

Finally, the direct calorimetric and gasometric researches of Howland[41] in Lusk's laboratory should be especially noted. In discussing the calculation of the body-surface, Howland cites the use of the factor 12.3 as a constant for infants, but we are not aware of any writers who have previously used this factor. The experiments were made with the respiration calorimeter[42] at the Cornell University Medical College in New York. Three infants under 1 year of age were studied and ocular observations of the activity of the infants were recorded.

Howland's experiments were subsequently published in detail and the results more fully discussed.[43] In this paper the relationship between body-surface and body-weight is extensively treated and the various factors and formulas are considered. A curve is proposed, which is represented by the algebraic expression $y = mx + b$, in which y is the surface area of the infant, x the weight of the infant in grams, m the constant 0.483, and b, 730 sq. cm.

The last portion of the paper, which is of most significance, compares the direct and indirect computation of the heat-production of the infants observed. This comparison is of such value to workers in metabolism that it is given here in Table 11. The agreement between the heat-production as directly measured and as indirectly computed is striking, to say the least, and justifies for the present the utilization of the indirect method of computing the calorimetry of infants.

Though Howland, using Lusk's calorimeter, has been eminently successful in experiments on the direct calorimetry of infants, experience with such researches in the Nutrition Laboratory has led us to believe that a type of calorimeter with less mass, less heat capacity, and probably not of the continuous-flow type could most advantage-

40. Bahrdt and Edelstein: Festschrift Dr. Otto L. Heubner, 1913, Berlin.

41. Howland: Proc. Soc. Exper. Biol. and Med., 1911, viii, 63; (Hoppe-Seyler's) Ztschr. f. physiol. Chem., 1911, lxxiv, 1.

42. Williams: Jour. Biol. Chem., 1912, xii, 317.

43. Howland: Tr. Fifteenth Internat. Cong. Hyg. and Demog., 1912, ii, 438. (Pub. Washington, 1913.)

ously be employed for the short periods necessitated by experiments with infants. Several types or modifications of calorimeters have been in process of testing for some time, and pending the satisfactory development, construction and testing of an infant calorimeter with the qualifications referred to, we have actively undertaken the study of infant metabolism as determined by indirect calorimetry. In these observations we have devoted our energies to the accurate measurement, in relatively short periods, of the carbon dioxid produced and oxygen consumed by infants less than 1 year of age.

TABLE 11.—HEAT-PRODUCTION OF INFANTS, DIRECTLY AND INDIRECTLY MEASURED, AS REPORTED BY HOWLAND

Subject	Food	Calories per Sq. M. per Day		Difference per cent.
		Measured	Calculated	
Child 1.....	Ordinary	1,046 1,113 1,196	1,084 1,174 1,164	2
Child 1.....	Nutrose added	1,218	1,179	3
Child 1.....	Nutrose added	1,204 1,235 1,181	1,180 1,212 1,250	1—
Child 1.....	Fasting	1,106 1,226 1,301	1,177 1,156 1,243	1—
Child 3.....	Ordinary	858 915	793 933	2
	Ordinary	825	840	2

INDIRECT CALORIMETRY

A number of physiologists have used the respiratory exchange to compute the total calorimetry by the method of so-called "indirect calorimetry."[44] From analyses of the urine and from a careful study of the respiratory exchange it is possible to apportion the catabolism between protein, fat and carbohydrate according to methods worked out most carefully by Zuntz and his associates. Having apportioned this catabolism, it is relatively simple to compute the total caloric output from the well-known heat of combustion of the various nutrients. Thus, for every gram of nitrogen in the urine, it has been definitely shown that 26.51 calories are developed; for every gram of carbo-

44. This method is not to be confused with the usage of certain French writers who consider "indirect calorimetry" as indicating the computation of material consumed by noting the weights of food eaten, excreta, and gain or loss of body-weight.

hydrate burned in the body, not far from 4 calories are produced, and for every gram of fat, 9.5 calories.[45]

A simpler method of computing the total heat, however, is to utilize the respiratory quotients, that is, the ratio between the carbon dioxid produced and the oxygen burned. Accordingly, if one knows exactly the respiratory quotient, the total carbon dioxid produced, and the oxygen absorbed, it is relatively simple to compute the total energy by using the so-called calorific equivalent for either carbon dioxid or oxygen. These calorific equivalents have also been most carefully studied by Zuntz and his associates, and as a result we have a very helpful table which gives the calorific equivalent of carbon dioxid with various respiratory quotients. When pure fat is burned, the respiratory quotient is not far from 0.71, and Zuntz has shown that for every liter of carbon dioxid produced by burning pure fat, 6.606 calories are liberated, or 3.363 calories per gram of carbon dioxid. On the other hand, when pure carbohydrates are burned, the ratio between carbon dioxid and oxygen is 1.00, that is, for every liter of carbon dioxid produced, 1 liter of oxygen is absorbed. Under these conditions Zuntz has shown that each liter of oxygen consumed corresponds to 5.047 calories, or 2.569 calories per gram of carbon dioxid.

TABLE 12.—Calorific Equivalents of Carbon Dioxid

Respiratory Quotient	Calorific Value of Carbon Dioxid		Respiratory Quotient	Calorific Value of Carbon Dioxid		Respiratory Quotient	Calorific Value of Carbon Dioxid	
	Per Liter cals.	Per gm. cals.		Per Liter cals.	Per gm. cals.		Per Liter cals.	Per gm. cals.
0.70	6.694	3.408	0.80	6.001	3.055	0.90	5.471	2.785
0.71	6.606	3.363	0.81	5.942	3.025	0.91	5.424	2.761
0.72	6.531	3.325	0.82	5.884	2.996	0.92	5.378	2.738
0.73	6.458	3.288	0.83	5.829	2.967	0.93	5.333	2.715
0.74	6.388	3.252	0.84	5.774	2.939	0.94	5.290	2.693
0.75	6.319	3.217	0.85	5.721	2.912	0.95	5.247	2.671
0.76	6.253	3.183	0.86	5.669	2.886	0.96	5.205	2.650
0.77	6.187	3.150	0.87	5.617	2.860	0.97	5.165	2.629
0.78	6.123	3.117	0.88	5.568	2.835	0.98	5.124	2.609
0.79	6.062	3.086	0.89	5.519	2.810	0.99	5.085	2.589
						1.00	5.047	2.569

An extremely simple method for calculating the catabolism, therefore, is to multiply the total amount of carbon or oxygen measured by the corresponding calorific equivalent. As a matter of fact, Zuntz in his work has used most frequently the calorific equivalent of oxygen, for in his method of studying the respiratory exchange the determina-

45. The heat of combustion of anhydrous cow's milk fat is 9.2 calories.

tions of oxygen are somewhat more exact than are those of carbon dioxid. Since, in our respiration apparatus, the carbon dioxid determinations for short periods are even more exact than are the determinations of the oxygen, we give in Table 12 the calorific equivalents of carbon dioxid with the varying respiratory quotients, particularly as this table will be used extensively in the computation of our own researches.

As any form of indirect calorimetry must of necessity be somewhat speculative,* one must always rely for fundamental values on direct heat measurements. Such measurements have been extensively made with men by Atwater and his associates at Wesleyan University, Middletown, Conn., where it was shown in experiments of long duration that the heat output as measured directly by the respiration calorimeter and the heat output as computed from the respiratory exchange agreed remarkably well. It should be pointed out, however, that these computations were based on twenty-four-hour periods. In certain experiments the computation has likewise been successful for periods as short as six hours, but it remained for Howland[46] to demonstrate with Lusk's calorimeter the complete agreement of the direct calorimetric measurements and of the computation from the gaseous exchange for short periods and particularly with an infant as subject. This being the case, the field is open for making a large number of metabolism experiments with the respiration apparatus in laboratories and institutions where a respiration calorimeter for direct calorimetry is not available.

BASAL METABOLISM

While the normal life of the infant is a relatively simple and constant one, yet it does include periods of muscular activity which vary greatly, the extremes ranging from perfect muscular repose during sleep to the violent exercise incidental to vigorous crying. As a result of these changes in muscular activity, the output of heat would likewise vary largely, with a minimum output during sleep and quiet and a maximum during the period of crying. An attempt has been made to find the average value for the heat output of an infant by

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46. Howland: Tr. Fifteenth Internat. Cong. Hyg. and Demog., Washington, 1913, ii, 451.

* It will be noted that in this paper the computation of the energy derived from protein is neglected and that the total energy output is computed only from the amounts of carbon dioxid and oxygen. The possible error in neglecting the protein has been computed by Magnus Levy to be somewhat under 1 per cent., and as the determinations of nitrogen were not feasible in our studies, we have used the method of simple computation from the gaseous exchange as recommended by A. Loewy: Oppenheimer's Handbuch der Biochemie, Jena, 1911, iv, 281. See, also, Magnus-Levy: von Noorden's Handbuch der Pathologie des Stoffwechsels, Berlin, 1896, i, 207.

experiments with twenty-four-hour periods, thus securing an average for the life of the day; but when one considers that the difference between the heat output in complete muscular repose during sleep and the heat given off when the infant is crying vigorously may be as great as 60 or more per cent., it will be seen that this method of averaging does not furnish information with regard to the minimum metabolism.

The muscular activity of infants is twofold: (1) internal muscular activity, consisting of muscular tonus, the movements of the organs of circulation and respiration, and possibly the processes of digestion; and (2) external muscular activity such as the movements of the limbs or vigorous body movement incidental to crying. The internal movements can be controlled only by minimizing the after-effects of digestion through the absence of food; the regular involuntary muscular activity of the respiratory and circulatory system and the muscular tonus cannot be altered. On the other hand, the external muscular activities are at a minimum only during complete muscular repose, as in deep sleep. It is thus seen that the ideal conditions for studying the basal or minimum metabolism of infants would be the postabsorptive state, that is, sufficiently long after the last meal to insure that there was no longer an absorption of food materials from the alimentary tract, and during deep sleep when there is complete muscular repose. With very young infants, periods of complete muscular repose cannot be expected for any great length of time, probably not for more than two successive hours.

We have, then, two factors to deal with: first, the heat elimination incidental to the specific catabolic stimuli of the food materials accompanying the digestion and absorption of food, and second, the internal muscular activity of the infant. If the first of these factors can be eliminated, we have what may properly be termed the basal metabolism unaccompanied by extraneous muscular activity of any kind.

Accordingly, in our first years of experimenting, we have based our study of the metabolism of infants on the careful determination of the carbon dioxid production and oxygen consumption of infants under one year in a special form of respiration apparatus, under conditions favoring the accumulation of accurate information regarding the basal metabolism.

RESPIRATION APPARATUS

The apparatus used in this research was a modified form of that briefly described by us in our first communication.[47] The essential modifications are, first, arrangements for continuous observations

47. Benedict, F. G., and Talbot, F. B.: Some Fundamental Principles in Studying Infant Metabolism, Am. Jour. Child. Dis., 1912, iv, 130.

whereby periods of any desired length can be secured, and, second and most important, the method of determining the oxygen consumption directly. The apparatus has been carefully controlled by burning known weights of alcohol, securing not only the respiratory quotients, but likewise the total amount of carbon dioxid and oxygen corresponding to the given amount of alcohol burned. For a complete description of this apparatus and tests made with it, reference may be made to the large publication previously referred to.[48] As the infant gives off carbon dioxid and consumes oxygen, the air leaving the chamber is rich in carbon dioxid and water-vapor from the lungs and skin of the

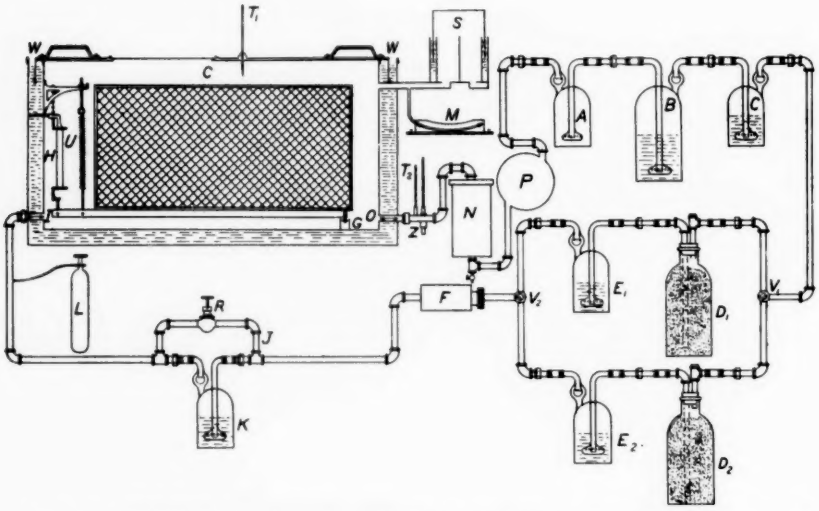

Fig. 1.—Detailed scheme of respiration apparatus. *C*, chamber; *W*, *W*, water jacket; *O*, outgoing air-pipe; *Z*, psychrometer; *N*, muffler; *P*, blower; *A*, acid trap; *B* and *C*, Williams water-absorbers; V_1 and V_2, 2-way valves; D_1 and D_2, carbon dioxid absorbers; E_1 and E_2, air-dryers; *F*, sodium bicarbonate can; *J*, by-pass; *R*, valve; *K*, air moistener; *L*, oxygen cylinder; *I*, ingoing air-pipe; *S*, spirometer; T_1 and T_2, thermometers; *M*, manometer; *U*, spiral spring; *H*, pneumograph.

infant, contains a normal amount of nitrogen, and is deficient in oxygen. By means of a rotary pump, the air is carried from the chamber and forced through sulphuric acid which absorbs the water, then through soda lime to remove the carbon dioxid; oxygen is next introduced and when the air returns to the chamber it is free from carbon dioxid and water and contains a normal percentage of nitrogen and oxygen. A scheme of this respiration apparatus, giving in considerable detail some of the special connections, may be seen in Figure 1.

48. Benedict, F. G., and Talbot, F. B.: Carnegie Institution of Washington, Publication No. 201, 1914.

METHOD OF RECORDING THE DEGREE OF MUSCULAR REPOSE

Special care was taken to secure graphic records of the degree of muscular repose of the infant, and each experiment in the entire series of some 1,200 periods, with about eighty infants, was accompanied by a graphic registration of the degree of muscular repose. This was accomplished by resting one end of the crib on a knife-edge bearing and suspending the other on a spiral spring, so that even the slight changes in the center of gravity of the infant would alter the tension on the spring. One end of a pneumograph was attached to the crib and the other end to the wall of the chamber, the pneumograph thus being parallel to the spiral spring. The slightest lengthening or shortening of the pneumograph produced a change in the tension of the confined air, these varying air tensions being transmitted by a tube through the walls of the chamber to a delicate tambour and pointer which gave graphic records on a kymograph drum. It is only necessary here to give one characteristic tracing, illustrating the records obtained by this method as to the degree of muscular repose. This curve, which is shown in Figure 2, was obtained Jan. 28, 1914, with G. M., an infant weighing 3.73 kg.

At the bottom of the figure is shown the record of the sensitivity test which precedes each experiment. In these tests, weights equal to the weight of the infant are placed in the crib; a 50-gm. weight is then dropped from a height of 21 cm. so as to strike the crib a blow at approximately 32 cm. from the knife-edge bearing on which the crib rests, thus giving an impulse to the crib, the vibrations gradually slowing down. Tests are made with the kymograph set first at slow speed and then at fast speed. In the record of the experimental period, the major movements are shown by the larger amplitude. It will be seen that the infant quieted down sufficiently to begin the first period of the experiment at 3:05 p. m. Aside from the slight movements at the end of the period, the infant was very quiet until 3:28 p. m. In the period from 3:28 p. m. to 3:59 p. m., there were several major movements and toward the end of the next period the infant was obviously very restless. This curve is of particular interest in that it shows in the period from 4:23 p. m. to 4:50 p. m. the movements of the crib incidental to hiccoughs. Indeed, it is possible so to adjust the sensitivity of the crib as to record the respirations.[49]

At first the infant was observed through the window in the cover of the apparatus to see whether or not he was quiet. While the ocular method of recording changes in position and the activity of an infant

49. Benedict, F. G., and Talbot, F. B.: Carnegie Institution of Washington, Publication 201, 1914, p. 58 (Fig. 6).

is much to be preferred to the terse statements usually accompanying reports of metabolism experiments to the effect that the animal, infant or person was "quiet," "fairly quiet" or "restless," yet such observa-

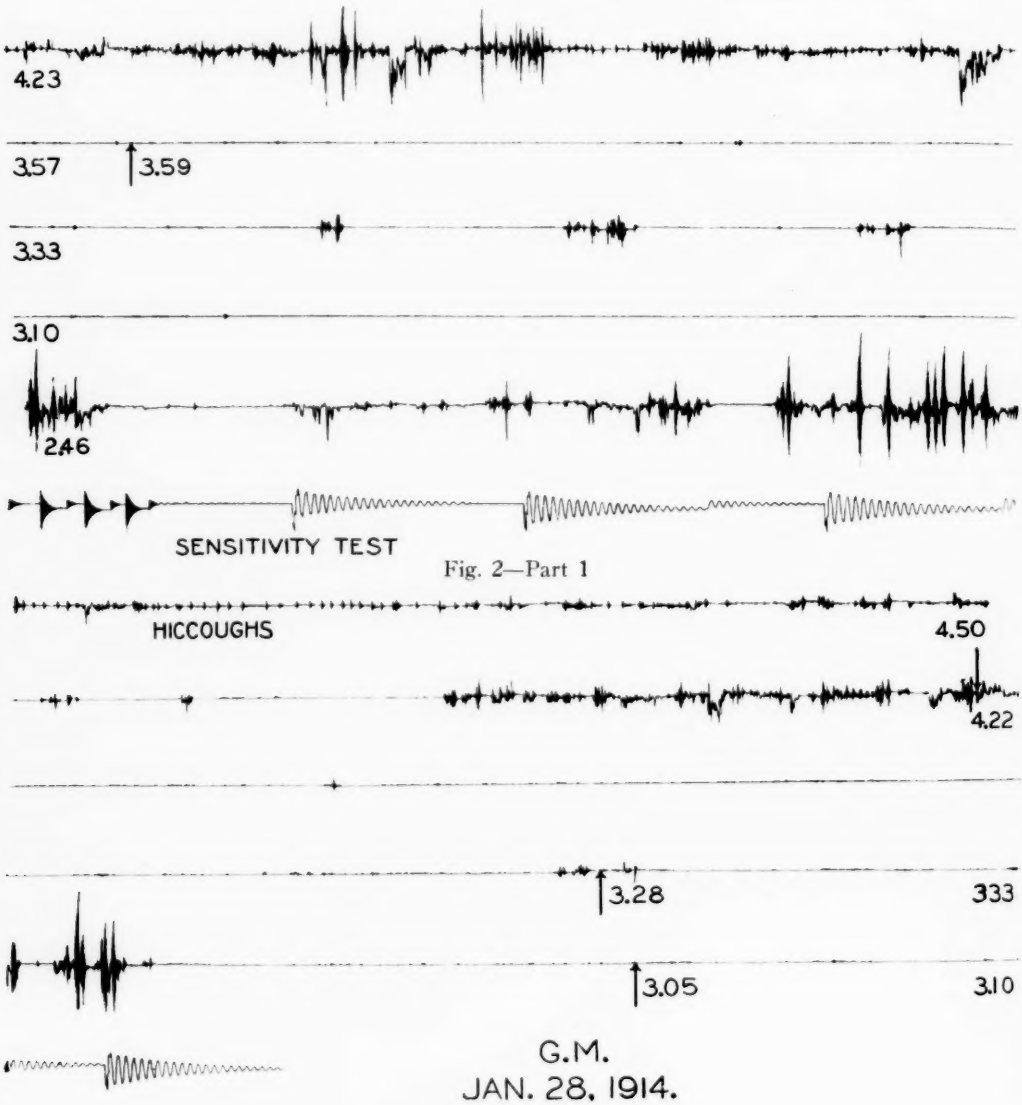

Fig. 2—Part 1

Fig. 2—Part 2

Fig. 2.—Typical kymograph curve, showing sensitivity test and records of muscular activity.

tions cannot be relied on. We have repeatedly seen experimental periods when a careful observer, even though watching the infant continuously, was unable to record a perceptible movement other than

those of respiration, and yet the suspended crib, pneumograph and tambour have recorded distinct and persistent muscular tremors, accompanied in all cases by an increasing pulse-rate and increased metabolism as measured by the carbon dioxid production and oxygen

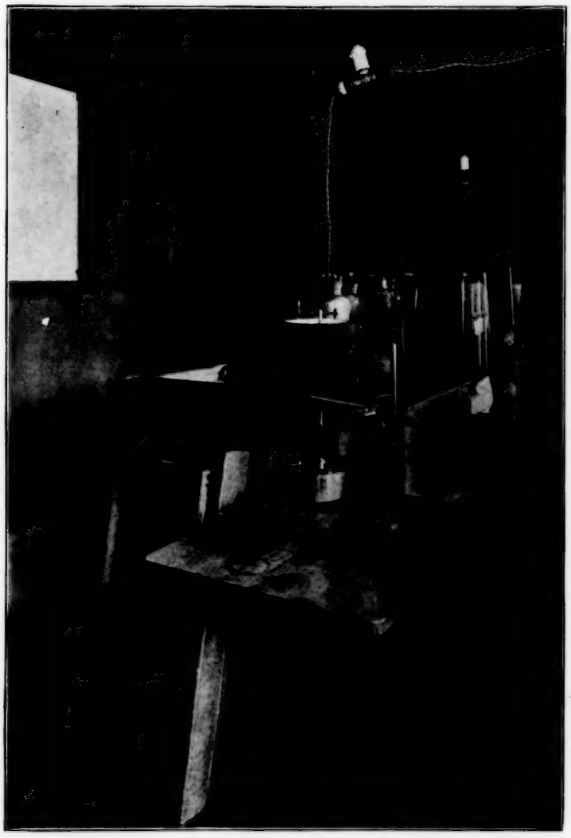

Fig. 3.—General view of the infant respiration apparatus. In the foreground is the respiration chamber showing the crib inside. The cover of the chamber rests on the floor, and through the glass window may be seen the earpieces of the stethoscope used for recording the pulse-rate. On the shelf in front of the chamber are the tambour and kymograph for the graphic records of movements. Directly behind the chamber are the hygrometer, the gas meter immersed in water, and the cylinder of oxygen, while in the rear the spirometer may be seen at the right and the sulphuric acid and soda lime containers of the absorbing system at the left. In the corner of the room is the balance for weighing the absorbing system.

consumption. The visual estimation was therefore discontinued as being too inaccurate and unreliable a record of the degree of quiet.

The length of a period of observation depends altogether on the muscular repose of the infant, as only quiet periods, accompanied by

a low pulse-rate, are of value. With a small, quiet infant, the periods may vary in length from twenty to thirty minutes, but with a large infant they may be as short as fifteen minutes.

The respiration apparatus as installed in the Children's Department of the Massachusetts General Hospital is shown in Figure 3. It consists of the respiration chamber, with oxygen supply, meter, balances for weighing, air-purifying apparatus, barometer and tambour and kymograph for recording the degree of muscular repose.

WARD CRIB RECORDER

The relationship observed between the graphic tracings of the muscular activity and the catabolism indicated the possible value of recording the activity of the infant throughout the day when it was not inside the respiration chamber. Accordingly, to assist in settling

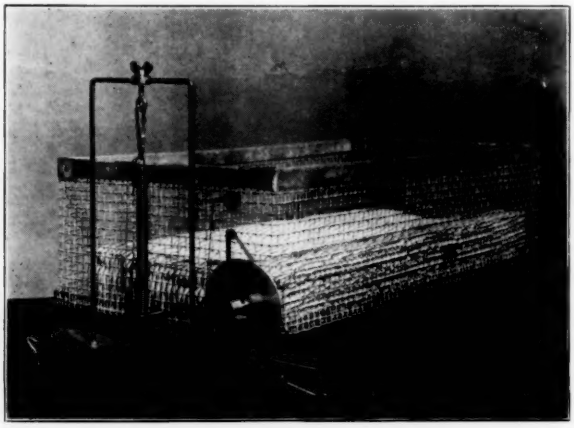

Fig. 4.—Ward crib recorder.

some complicated problems of nutrition, a special apparatus, embodying the suspended crib principle, was devised and set up in the children's ward of the hospital in order to obtain a continuous graphic record of the muscular activity of the infant (Fig. 4).

In this apparatus the wire crib rests at the rear end on two steel points fitting into steel cups. The front end is suspended by a spring with link chain adjustment for height. At the right of the front end is an aluminum wheel attached to a revolution counter. A fine thread fits in a groove on the edge of this wheel. One end of this thread is attached to the upper end of the cage and the other end to a fine spiral spring, projecting to the right of the revolution counter. Each movement of the cage in a vertical direction moves the revolution counter, and as the cage descends, the fine spring keeps the tension on the

thread tight. The pawl on the top prevents backward motion of the wheel and the pawl-standard serves as a pointer to read fractions of the circumference of the wheel.

METHOD OF RECORDING THE PULSE-RATE

Previous experiments with adults in the Nutrition Laboratory, in which the large respiration chambers were used, showed a striking relationship between the pulse-rate and the metabolism. Attempts were accordingly made to secure accurate pulse-records in our observations with infants. For this purpose we attached the bell of a small Bowles stethoscope to the infant over the apex-beat of the heart by means of strips of adhesive plaster. A rubber tube connecting with the bell led to a pipe in the wall of the chamber, a piece of rubber tubing and earpieces being attached to the outer end of the tube. Even with a total length of some 2 or 3 meters from the bell to the earpieces, it was possible to count the pulse-rate of the weakest infant. Throughout the entire period of observation, the pulse-rate was recorded every two minutes by an assistant who made this her sole duty.

We are far from satisfied with this as a permanent method for securing a record of the pulse-rate, and it is our hope, in connection with the hospital or with the laboratory, to secure records either with the string galvanometer or with the Bock-Thoma oscillograph. It is clear that the records of the pulse-rate should be more objective than they can be even with a specially detailed assistant.

SELECTION OF SUBJECTS

The infants studied were either from the Children's Department of the Massachusetts General Hospital or from the Boston Lying-In Hospital. The routine histories, records of the physical examinations, notes regarding the urine, stools, blood and temperature, the pulse and respiration charts, and detailed records of the food were kept for all of the infants. The Wassermann reaction and the von Pirquet skin tests were also made in many cases. It does not seem desirable to publish the detailed hospital record of each infant that came under observation, especially since most of the evidence is negative as to whether or not an infant is normal. The clinical status of each infant is, however, given in Table 13.

In this table the term "infantile atrophy" is applied to the condition of an emaciated infant with such severe indigestion that it is unable to digest weak mixtures of cow's milk, with no gain in weight, and with a subnormal body-temperature. The convalescent stage of infantile atrophy is that in which the same infant subsequently begins to digest its food and to gain weight and has a normal temperature. Under-

TABLE 13.—Clinical Status of Infants Studied

Name	Age During Metabolism Observation	Clinical Status
F. B.	5½ mos...	Convalescent stage infantile atrophy.
M. A.	9 mos...	Under weight, splenic tumor, with anemia.
J. B.	5 mos...	Congenital syphilis, convalescent stage infantile atrophy.
L. B.	4 mos...	Under weight.
L. R. B.	4–4½ mos...	Normal infant.
A. C.	1½ mos...	Slightly under weight.
M. C.	4 mos...	Normal infant or slightly under weight.
A. D.	4–5 mos...	Convalescent stage, infantile atrophy.
M. D.	2–3 wks...	Normal infant.
R. E.	4½ mos...	Under weight or slightly under expected weight.
E. F.	3 mos...	Normal infant.
E. G.	10 mos...	Normal infant.
E. K.	17 mos...	Much under weight; rachitis, recovering from broncho-pneumonia.
F. K.	7 mos...	Under weight.
A. L.	3½–4 mos...	Under weight.
E. L.	4 mos...	Under weight, otitis media.
R. L.	6½–9 mos...	Approximately normal; later, under weight.
D. M.	11 mos...	Much under weight, rachitis.
F. M.	4–5 mos...	Under weight, congenital syphilis.
J. M.	8 mos...	Under weight, otitis media, rachitis.
M. M.	4½ mos...	Under weight following an acute indigestion.
E. N.	6–6½ mos...	Under weight.
L. O.	5–6 mos...	Infantile atrophy.
J. P.	6½–7 mos...	Under weight, gaining weight rapidly.
W. P.	5–5½ mos...	Under weight.
D. Q.	4½ mos...	Under weight.
E. R.	3 mos...	Under weight (slightly).
K. R.	4 mos...	Infantile atrophy.
A. S.	3 mos...	Normal infant, weighing more than the average.
E. S.	5 mos...	Infantile atrophy.
E. H. S.	2½–4 mos...	Infantile atrophy.
G. S.	2½ mos...	Under weight.
J. S.	5–6 mos...	Infantile atrophy (?) (temperature not subnormal).
P. S.	12 mos...	Under weight.
H. T.	5½ mos...	Normal infant, weighing more than average.
J. V.	3½–9 mos...	Prematurity; congenital syphilis; infantile atrophy in subnormal temperature and convalescent stage.
P. W.	7 mos...	Normal infant.
New Series		
R. A.	7 mos...	Moderately underweight.
E. C.	2½ mos...	Moderately under weight with indigestion.
H. C.	5 mos...	Much under weight.
O. C.*	5 hrs.–3 das.	Normal infant.
R. C.*	1–2 days...	Normal infant.
T. C.	8½–9 mos...	Much under weight.
B. D.	2 mos...	Normal infant. Breast fed.
F. D.	2½ mos...	Congenital syphilis. Normal weight.
N. D.	7 mos...	Moderately under weight.
R. D.*	2–5 days...	Normal infant of average weight.
B. F.	7 mos...	Moderately under weight.
U. H.*	3–28 hours.	Normal infant.
T. K.*	7–32 hours.	Normal infant.
L. L.	2–2½ mos...	Normal infant.
E. M.	8 mos...	Moderately under weight.
G. M.	6–6½ mos...	Much under weight. Eczema. Indigestion.
C. N.	4½ mos...	Eczema. Much under weight with indigestion.
I. N.	2–4 days...	Normal infant.
J. O.	4½ mos...	Pyloric spasm. Indigestion. Much under weight.
E. P.	11–14 days...	Normal infant.
F. R.	1–11 days...	Normal infant. Much above average weight.
I. R.	6–7 days...	Normal infant.
R. S.	9½ mos...	Normal infant. Much over average weight.

*These infants were obtained through the courtesy of the visiting physician of the Boston Lying-In Hospital, Dr. Charles Mon traville Green.

weight infants are those who are 0.5 kg. or more below the average weight for their respective ages, but whose digestion is not so severely deranged as those with infantile atrophy. This group includes all infants not classified as normal, or with infantile atrophy, or in the convalescent stage of infantile atrophy.

DISCUSSION OF RESULTS

In all of the researches carried out in the Nutrition Laboratory, particularly in studying pathologic cases, the want of suitable and adequate control data for comparison has been evident. With infants, particularly, the absence of normal controls is unfortunate. This led us to believe that our best service to pediatrics would be to determine the normal metabolism of infants. Accordingly, while a few observations were made on distinctly pathologic cases other than atrophic, our data were secured for the most part with normal or underweight infants.

One of the most important problems in such an investigation is the relationship between muscular repose and metabolism. In our first communication to this journal, we emphasized the importance of this relationship and pointed out the great service rendered by the graphic registration device for recording the muscular movements of the infant. Our consistent use of this device in all of our experiments furnished us with data in regard to the relationship between muscular repose and metabolism, which was accordingly made the subject of special study in this investigation.

In this research, also, it was hoped that some information would be gained as to the cause for variations in the metabolism of the infant; with this in view, a study was made of the possible relationships between the metabolism and the body-surface and the metabolism and the active mass of protoplasmic tissue.

1. Pulse-Rate

The careful observations of pulse-rate made while the subjects were inside the respiration chamber verified completely the twelve-hour observations made in the ward and published in our earlier paper. These showed very considerable fluctuations in the pulse-rate coincident with changes in muscular activity, such as change in body position, particularly in crying and immediately after nursing, so far as the movements inside the respiration chamber approximated those noted in the ward. For an elaborate series of observations on the pulse-rate as affected by the muscular activity incidental to a night's sojourn in the wards, our earlier paper may be consulted, as well as a number of records given more recently in the Carnegie Institution of Washington publication.

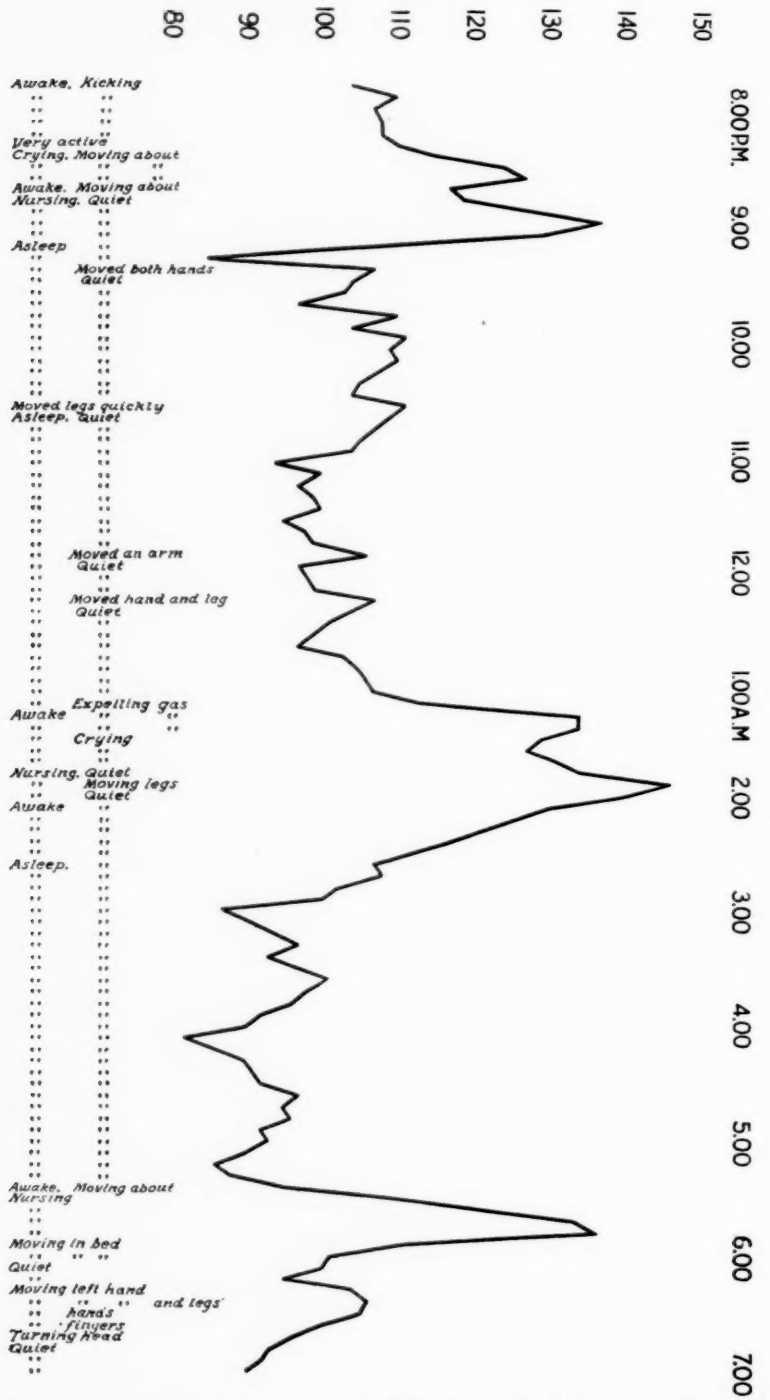

Fig. 5.—Pulse-rate curve for Tremballe, July 12, 1911. Age, 5 months; weight, 5.7 kg.

The surprising changes in pulse-rate found in the course of an ordinary night's sleep in the ward are shown in Figure 5 by the typical curve for the 5-months-old infant, Tremballe. Accompanying the curve are statements with regard to the condition and activity of the child. Tremballe was under observation in the ward from 7:40 p. m. until about 7 a. m., and for the greater part of this time was asleep. The pulse-rate varied from a maximum of 147 to a minimum of 83. During the latter part of the night the minimum record showed an average of not far from 90. An immediate and rapid effect on the pulse following changes in muscular activity is strikingly shown with this infant in every instance.

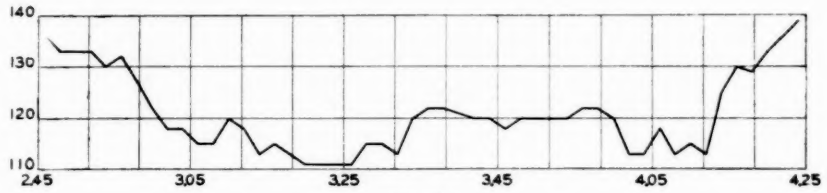

Fig. 6a

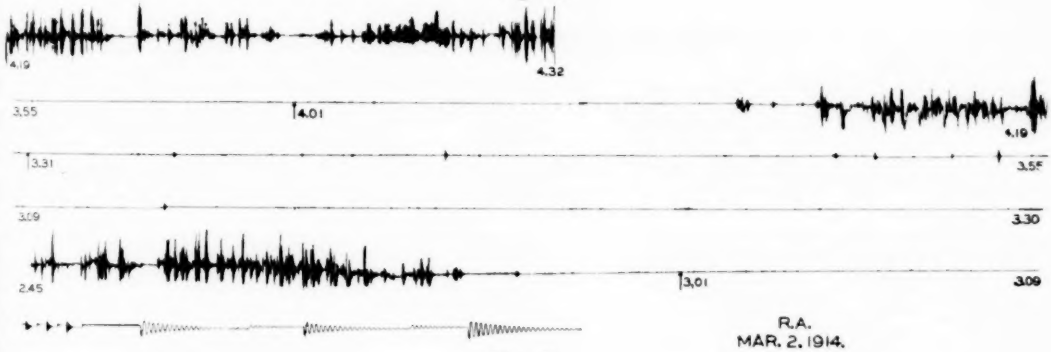

Fig. 6b

Fig. 6.—Pulse-rate and kymograph curves for R. A., March 2, 1914.

2. Relationship Between Pulse-Rate and Muscular Activity

While the observations made in the ward during the night experiments in 1911 showed conclusively the intimate relationship between pulse-rate and activity, this is even more strikingly brought out by the kymograph pictures obtained while the infant was inside the respiration chamber. With each change in bodily activity, there was obviously a noticeable change in the course of the kymograph record, and by means of frequent pulse-counts, we were able to make sharp comparisons between these two factors. A curve showing graphically the pulse-counts obtained in a typical experiment with R. A. on March 2, 1914, is given in Figure 6. For comparison, the kymograph record, somewhat reduced, is also given.

In comparing the two curves, we find that the period of considerable activity from 2:45 p. m. until about 2:58 p. m. is accompanied by a high pulse which fell rapidly as the infant quieted down. From 3:01 p. m. to 3:30 p. m., the kymograph curve shows a straight line, with but one or two slight movements. From 3:31 p. m. to 3:55 p. m., there is distinct evidence of slight restlessness, which is also apparent in the increased pulse-rate, this period being followed by complete repose from 3:55 p. m. to about 4:10 p. m., and a lowering of the pulse-rate. From that time until the end of the experiment, there is great activity and disturbance, with a rapidly rising pulse-rate. It is thus seen that the kymograph curve and the pulse-rate curve follow each other with great regularity.

3. *Relationship of the Muscular Activity, Pulse-Rate and Metabolism*

The noticeable influence of even minor muscular activity on metabolism makes it important to note that in all experiments in which the basal metabolism is to be determined, that is, in experiments that

TABLE 14.—COMPARISON OF THE PULSE-RATE, METABOLISM, AND MUSCULAR ACTIVITY IN OBSERVATION WITH M. M., JUNE 5, 1913

Period	Total Heat-Production per 24 Hours	Pulse-Rate	Activity
3:12 p. m. to 3:40 p. m.*	365	107	V
3:40 p. m. to 4:10 p. m.	276	93	I
4:10 p. m. to 4:31 p. m.	307	96	III
4:31 p. m. to 4:58 p. m.	288	90	II
4:58 p. m. to 5:23 p. m.	367	113	VI

* Preliminary period.

may subsequently be employed for comparison of normal individuals with pathologic cases, only periods of complete muscular repose should be used. It is obviously impossible to compare a quiet, resting, normal child with a sick, restless child, or vice versa. The difficulties incidental to securing such periods are known only to those who are actively engaged in this sort of experimenting, for a very large percentage of the results of experimental work may not be used, owing to changes in the extraneous muscular activity. Writers have, as a rule, attempted to indicate in a general way the results of certain experiments which cannot properly be included in comparisons by recording in some general terms the degree of activity of the child, stating whether it is awake or asleep, or comparatively quiet, or quiet,

etc. In recent years Schlossmann and Murschhauser have adopted a more elaborate system of ocular records, stating exactly what the infant is doing. After comparing the various methods of recording the degree of muscular repose, we have definitely adopted the suspended crib and kymograph.

It is clearly impracticable to reproduce in this publication all of the kymograph curves secured in our researches, but a comparison may be made of the muscular activity, the pulse-rate, and the metabolism in a typical experiment—that with M. M. on June 5, 1913—by reference to Table 14. In this table are given a record of the pulse-rate, the metabolism computed on the basis of the total heat output for twenty-four hours, and an estimate of the activity based on the following classification:

I. Very quiet, probably asleep.
II. Slight movements, few in number.
III. Some activity, but generally quiet.
IV. Moderately active.
V. Distinctly active.
VI. Very active, most or all of the time.

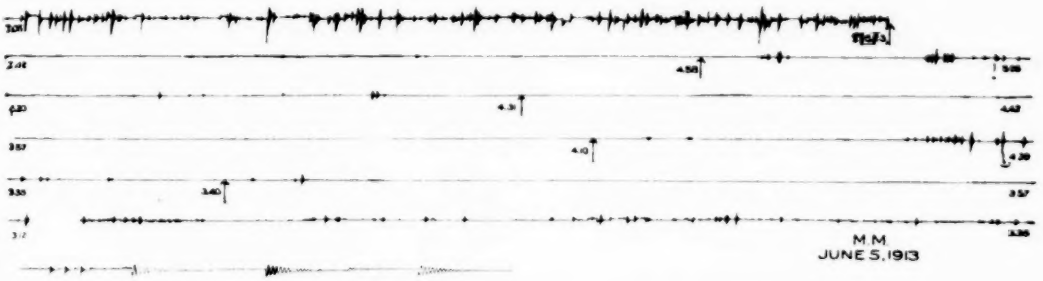

Fig. 7.—Kymograph curve for M. M., June 5, 1913.

The kymograph curve for the same experiment, which is reproduced in Figure 7, will give an illustration of the method of estimation we are using. This curve has certain striking points, inasmuch as the minimum and maximum activity are very well shown. During the preliminary period from 3:12 p. m. to 3:40 p. m., the infant was somewhat restless, quieting down sufficiently about 3:35 p. m. to justify the beginning of a new period at 3:40 p. m. As a matter of fact, the infant was so quiet in the next period that the activity can be characterized as I (Table 14). The activity in the last period, that is, that from 4:58 p. m. to 5:23 p. m., was sufficiently great to be classified as VI. This curve shows clearly the futility of attempting to graduate by kymograph records the exact degree of the activity and the heat-production, for although the curve appears to indicate

that the activity in the last period (from 4:58 p. m. to 5:23 p. m.) was much greater than that in the preliminary period from 3:12 p. m. to 3:40 p. m., the metabolism is very nearly the same and the pulse-rate is only 6 beats higher in the last period. This also justifies the statement that the measurements obtained in preliminary periods are not sufficiently reliable to admit of extended discussion. The fact that no greater metabolism is shown in the last period than in the preliminary period, although the activity appears to be greater, should therefore be considered as a deduction based on single measurements in two individual periods, either of which may be liable to error. Furthermore, when comparing the pulse-rates it should be stated that although the average pulse-rate in the preliminary period was 107, the individual counts ranged from 95 to 120, while the pulse-rates in the last period, although the average was 113, actually varied from 93 to 124. Discrepancies such as these serve again to emphasize the fact that only periods of complete muscular repose can logically be used in discussing infant metabolism.

4. Significance of the Relationship

From the preceding discussion the conclusion may be drawn that only periods of complete muscular repose may be used in comparing the results obtained with different individuals and with the same individuals on different days. The total catabolism of the infant is the resultant of two factors: first, the metabolism due to the internal activity incidental to circulation and respiration and the general muscle tonus of the body, that is, maintenance metabolism; second, the metabolism due to the external muscular activity, which may vary from slight movements of the hand or fingers to violent movements incidental to severe crying.

The external muscular movements are recorded with considerable fidelity on the kymograph drum by means of the registering apparatus described, but we have seen that this record does not give a comparative picture of the degree of activity of different infants. Consequently for comparing the maintenance metabolism only periods in which the external muscular activity is eliminated should be used, since in the last analysis, knowledge with regard to internal muscular activity is desired, uncomplicated by the increased metabolism due to external muscular activity. We believe that our evidence justifies us in asserting that we have two admirable indices for securing these ideal conditions of muscular repose for comparison, first, the graphic records obtained with the kymograph, and second, the pulse-rate. For comparing the metabolism of different infants, therefore, only those periods with records of complete muscular repose and with a minimum pulse-rate can legitimately be employed.

5. Relationship between Pulse-Rate and Metabolism

From the general pictures of the kymograph curves and the pulse-curves, one may infer that the pulse-rate follows closely the muscular activity. Furthermore, since it has been shown that the relationship between the metabolism and the kymograph curves is comparatively constant, it is reasonable to expect that the pulse-rate will follow the metabolism. That this latter relationship is usually more nearly constant than the relationship between the metabolism and the record of the muscular activity is clearly indicated in a number of observations in which the kymograph record showed a complete absence of extraneous muscular activity while the pulse-records showed fluctuations.

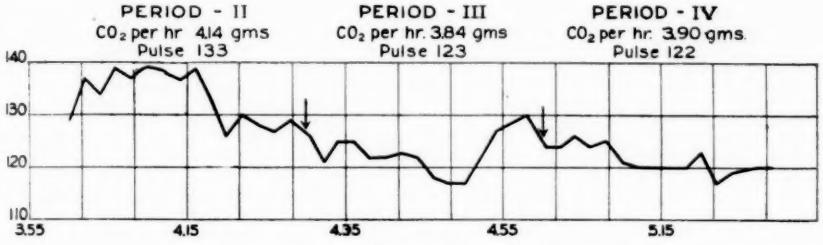

Fig. 8a

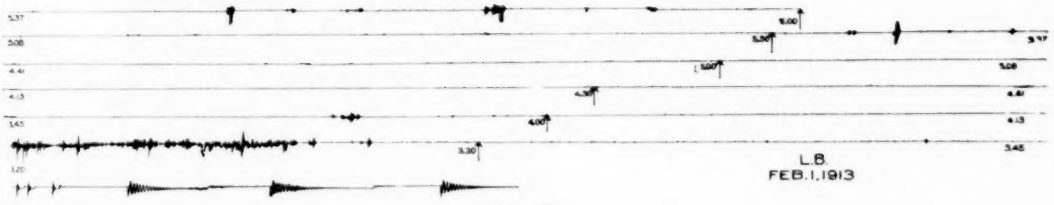

Fig. 8b

Fig. 8.—Pulse-rate and kymograph curves for L. B., Feb. 1, 1913.

An excellent illustration of this may be seen in the pulse and kymograph curves which were obtained in the observation of Feb. 1, 1913, with the infant L. B. (Fig. 8). Thus between 4 p. m. and 5:30 p. m., one may assume that the activity was essentially of Grade I, that is, minimum. Nevertheless the pulse-rate is considerably higher in the period between 4 p. m. and 4:30 p. m. than in the two following periods, as is shown by the pulse-curve and the figures for the pulse-rate per minute. As a matter of fact, the total metabolism is likewise higher in the first period as is evidenced by the carbon dioxid output per hour which is given on the pulse-curve. In this curve, therefore, which excludes the extraneous activity, we find the pulse-rate following very closely the total metabolism. While the kymograph

curve did not indicate muscular activity, nevertheless the pulse-rate gave evidence of an increased internal activity.

6. Basal Metabolism of Infants Studied

In the beginning of this research on infant metabolism, one of the fundamental questions which presented itself to us with special force was as to what may be considered the normal basal metabolism of infants. Consequently we made it our aim to study as many infants as possible and to secure a sufficient number of periods of complete repose on a sufficient number of days to establish beyond reasonable doubt the basal metabolism of each infant. The infants secured for these observations varied sufficiently in age, weight, height, and sex to permit a comparative study of the results as to the constancy or lack of constancy in the metabolism.

A. Selection of Data Used for Comparison

From the data obtained a table has been compiled which gives the average results of the periods with each infant in which the metabolism was at a minimum (Table 15). The selection of the periods was based on the records of the pulse-rate and the muscular activity, only such periods being used as showed a normally low pulse-rate and practically no muscular activity, that is, those characterized as I or II. Of the eighty-three infants studied thus far in this research, but sixty were used in the comparison of the metabolism of different infants and but 360 periods out of the 1,250 periods were available for the comparison. The data are arranged according to the increasing weights of the infants. Since with one infant, J. V., the studies continued over a period of several months, the average minimum metabolism is given for periods secured at an early age, and again for periods obtained several months later. Various bases of comparison may be used, but in this table the infants have been compared on the basis of the energy transformation in twenty-four hours.

In employing the data in Table 15 for the discussion of the fundamental questions considered, it is necessary to emphasize the fact that the amount of material and the method of its selection justify its use for a basis of comparison.

The number of infants (sixty in all) permits extended comparison and discussion.

Furthermore, the data are sufficiently extensive for each subject, as an examination of the table will show that in all but two instances, at least two periods are used for securing the average value for each infant; in other words, the values were determined in duplicate. In many cases the number of periods for comparison greatly exceeded

this; for example, in one instance twenty-two periods were available for averaging.

Obviously no infant lives on a minimum metabolic plane throughout the entire twenty-four hours; indeed, but a small proportion of the total number of the experimental periods could be utilized for this important comparative study. Nevertheless, since in but two instances was it necessary for us to rely on the computation of the minimum metabolism of the infant from one experimental period, and in only one other instance were our data limited to those secured in two periods on one day, we believe that we have obtained a reasonably accurate estimate of the minimum metabolism of each infant which justifies critical study and comparison.

B. Minimum Influence of Food

In discussing our results, the criticism can be raised that one of the factors outlined in our definition of basal minimum metabolism was not so strictly observed in this study as could be desired in that the infants were rarely in the postabsorptive state, since the observations were for the most part made from one to one and a half hours after the ingestion of food.

It has clearly been shown in experiments on men and animals that the ingestion of a mixed diet results in an increased metabolism. When isolated nutrients are ingested, the greatest increase has been observed with protein. With fat there is relatively but little, if any, increase. With carbohydrates, while investigators differ as to the quantitative relationships, it has been observed with men in this laboratory that cane-sugar and levulose may stimulate the metabolism to a degree comparable with that resulting from the ingestion of an equivalent weight of protein. On the other hand, lactose—the chief carbohydrate in the diet of infants—has a minimum influence on the metabolism.

This criticism of our experiments has, therefore, considerable theoretical importance, but practically we must consider the fact that the diet of the infant is of such a character as to produce a minimum amount of increase in the metabolism. With infants a large proportion of the protein ingested—some 60 per cent. or more—may be stored in the body, and Rubner has shown that this storage does not affect the total metabolism. Since the protein ingested by the infant rarely exceeds 15 per cent. of the total energy requirement of the body,[50] it can be seen that we may expect from this nutrient only the minimum influence on the heat-production of infants. Fat has admittedly but a slight influence, while the predominating carbohydrate—milk-sugar or lactose—has likewise only a minimum influence.

50. Rubner: Sitzber. k. Preuss. Akad. Wissensch, 1911, xx, 440.

Subject	Sex*	Body-Weight Without Clothing kg.	Height cm.	Age	Days Included in Average	Periods Averaged	Carbon Dioxid per Sq. Meter (Meeh) per Hr.† gm.
J. V.	♀	1.94	47	3½ months	2	3	12.1
E. H. S..	♂	2.96	51	3½ months	5	8	11.6
A. C. ...	♀	2.99	..	1½ months	3	8	9.7
E. S.	♀	2.99	..	5 months	3	6	14.0
A. D. ...	♀	3.16	56	4½ months	5	15	13.0
K. R. ...	♂	3.17	56	4 months	2	4	12.1
A. L. ...	♀	3.18	53	4 months	2	2	12.4
L. O. ...	♂	3.18	..	6 months	7	12	15.3
J. B.	♂	3.23	..	5 months	2	4	13.3
G. S.	♂	3.30	..	2½ months	3	5	12.1
R. D. ...	♀	3.31	47	3 days	4	5	7.1
J. V.	♀	3.38	53	8½ months	3	3	16.7
H. C. ...	♀	3.42	55	5 months	2	4	15.2
O. C. ...	♂	3.45	51	2 days	3	6	7.8
J. O.	♀	3.53	57	4½ months	2	6	13.8
T. K. ...	♂	3.60	53	19 hours	2	3	7.5
I. N.	♂	3.65	52	3 days	3	5	7.5
F. M. ...	♂	3.65	..	4½ months	3	5	15.4
E. C.	♂	3.70	57	2½ months	3	5	13.9
E. P. ...	♀	3.71	51	12½ days	2	4	7.9
G. M. ...	♀	3.73	58	6 months	4	8	15.2
I. R.	♂	3.89	52	6½ days	2	2	10.3
M. D. ...	♂	3.99	..	17 days	2	4	9.2
U. H. ...	♂	4.00	53	15 hours	2	2	7.4
L. B. ...	♀	4.04	..	4 months	3	8	13.2
R. C. ...	♀	4.13	51	37½ hours	2	4	7.9
E. L. ...	♂	4.15	59	4 months	1	2	14.0
W. P. ...	♂	4.31	..	5 months	2	6	14.6
F. R. ...	♂	4.40	52	6 days	6	8	8.6
J. S.	♂	4.41	63	5½ months	5	7	15.6
E. R. ...	♂	4.49	55	3 months	3	5	12.0
T. C. ...	♂	4.72	66	8½ months	5	10	15.5
C. N. ...	♀	4.74	63	4½ months	2	6	13.6
F. D. ...	♂	4.80	59	2½ months	1	2	12.4
F. B.	♂	4.87	60	5½ months	4	13	15.7
B. D. ...	♀	4.90	58	2 months	2	4	10.5
R. E. ...	♂	5.04	60	4½ months	3	7	12.2
L. L.	♂	5.13	57	2½ months	10	13	10.6
D. M. ...	♂	5.18	66	11 months	2	2	15.0
D. Q. ...	♂	5.28	62	4½ months	2	4	11.9
E. N. ...	♀	5.40	66	6 months	7	22	13.9
J. P.	♂	5.45	63	7 months	4	7	15.3
M. M. ..	♀	5.47	62	4½ months	3	7	10.6
J. M. ...	♂	5.63	62	8 months	2	6	18.2
M. A. ...	♂	5.67	68	9 months	4	9	12.9
F. K. ...	♂	5.71	65	7 months	6	8	14.2
B. F.	♀	5.72	64	7 months	2	5	14.9
L. R. B..	♀	5.99	64	4 months	4	11	11.3
A. S. ...	♂	6.02	63 (?)	3 months	1	1	10.6
M. C. ...	♀	6.17	63	4 months	3	7	11.9
E. M. ...	♂	6.19	63	8 months	2	2	18.7
R. A. ...	♀	6.42	65	7 months	2	3	12.4
N. D. ...	♀	6.79	67	7 months	3	5	12.3
P. S.	♂	6.80	67	12 months	3	10	14.4
E. F. ...	♂	7.07	62	3 months	2	2§	10.2
P. W. ...	♂	7.11	64 (?)	7 months	2	5	14.2
R. L. ...	♂	7.58	71	8½ months	5	8	13.9
E. K. ...	♂	8.03	73	17 months	1	2	14.2
H. T. ...	♂	9.33	75 (?)	5½ months	1	1	12.4
E. G. ...	♂	9.37	74	10 months	3	5	11.4
R. S.	♂	9.94	74	9½ months	2	4	13.4

* In this column ♀ means female and ♂ male.

† In accordance with the usage of European writers, we give these values, although we

‡ See page 15.

§ The activity estimated for these two periods was II and III, respectively.

Oxygen per Sq. Meter (Meeh) per Hour gm.	Heat Produced					Average Rectal Temperature During Respiration Periods		Pulse-Rate
	Per 24 Hrs. cals.	Per Kilogram per 24 Hours cals.	Per Square Meter per Twenty-Four Hours					
			Howland‡ cals.	Lissauer $\frac{3}{2}$ / $10.3\sqrt{w}$ cals.	Meeh $\frac{3}{2}$ / $11.9\sqrt{w}$ cals.	°C	°F	
10.8	164	85	984	1,032	882	....	....	129
9.6	194	65	891	906	783	36.8	98.2	109
8.0	163	55	756	759	660	37.2	98.9	126
11.0	225	75	1,036	1,048	911	36.5	97.7	107
10.7	229	72	1,010	1,026	895	36.5	97.7	114
10.2	213	67	936	960	829	36.6	97.8	103
10.7	226	71	996	1,020	876	36.8	98.3	107
12.1	260	82	1,154	1,172	1,008	36.9	98.5	106
10.2	223	69	978	996	854	36.1	97.0	95
10.0	216	65	931	946	818	36.9	98.4	119
6.8	146	44	632	641	554	37.1	98.8	110
13.4	297	88	1,264	1,280	1,108	37.3	99.1	126
12.6	280	82	1,184	1,199	1,039	37.3	99.2	113
8.0	168	49	703	714	618	36.9	98.4	129
11.2	255	72	1,051	1,069	925	36.8	98.2	104
7.0	158	45	655	664	575	37.0	98.6	105
8.0	174	48	702	715	616	36.9	98.4	104
13.0	300	83	1,219	1,238	1,064	37.1	98.8	118
11.3	267	72	1,068	1,085	939	37.4	99.4	122
7.5	169	46	672	683	590	36.8	98.3	119
12.7	299	80	1,186	1,205	1,041	36.8	98.2	112
8.6	211	54	810	827	715	36.8	98.3	127
8.2	196	49	738	756	656	37.0	98.6	127
6.8	167	42	630	643	556	37.1	98.7	114
10.6	272	67	1,020	1,041	901	36.9	98.5	124
7.6	186	45	684	701	606	37.1	98.8	108
12.3	306	74	1,128	1,152	995	37.2	99.0	127
11.6	303	70	1,076	1,104	962	36.8	98.2	96
8.0	207	47	732	752	649	37.2	99.0	121
11.9	319	72	1,114	1,152	997	36.9	98.5	111
11.0	283	63	979	1,013	873	37.2	98.9	116
12.9	354	76	1,194	1,230	1,062	37.0	98.6	109
12.0	330	70	1,097	1,136	982	36.9	98.4	116
11.0	303	63	999	1,033	892	37.7	99.8	115
13.1	370	77	1,211	1,257	1,082	37.2	98.9	111
9.8	274	57	898	927	802	37.7	99.8	122
11.3	324	64	1,035	1,070	919	37.1	98.7	114
9.4	269	52	844	878	759	37.3	99.1	119
12.5	369	71	1,152	1,188	1,034	37.3	99.1	119
10.1	305	57	930	972	846	37.3	99.1	101
11.7	353	66	1,069	1,117	962	37.1	98.7	111
13.0	387	70	1,152	1,207	1,039	36.8	98.3	105
9.7	285	52	854	891	770	36.8	98.2	96
15.1	467	83	1,368	1,432	1,239	37.2	98.9	112
11.7	356	63	1,037	1,085	939	36.9	98.5	105
12.6	381	67	1,107	1,158	1,003	37.2	98.9	109
12.3	386	68	1,115	1,165	1,016	37.1	98.7	109
10.4	331	55	923	973	844	37.2	99.0	106
9.5	305	51	840	888	774	37.3	99.1	113
10.1	333	54	912	967	837	37.1	98.8	103
16.2	535	87	1,452	1,540	1,334	37.4	99.4	130
10.5	358	56	940	1,002	868	37.4	99.3	118
11.1	381	56	965	1,032	893	37.2	99.0	100
13.3	453	66	1,133	1,219	1,058	36.8	98.2	100
8.7	311	44	756	828	708	37.1	98.8	111
12.2	439	62	1,061	1,147	998	37.1	98.8	120
12.2	455	59	1,038	1,140	991	37.4	99.4	115
12.9	497	62	1,092	1,212	1,044	37.7	99.9	105
9.5	420	45	816	912	797	37.2	98.9	101
11.4	479	51	922	1,046	907	37.2	98.9	106
11.5	531	53	971	1,115	965	37.3	99.1	108

believe they are peculiarly liable to misunderstanding and hence their use is unfortunate.

On these grounds, therefore, one would conclude that the total nourishment of the infant consists of material which for the most part does not tend to stimulate the metabolism greatly. On the other hand, so keen an observer as Schlossmann[51] states that the effect of the ingestion of food probably persists for some eighteen hours. Practically all of the investigators in metabolism have concluded that with adults, unless the diet is abnormally rich in protein, the metabolism reaches the basal line twelve hours after the last meal.

In our studies, while it was impracticable to secure the metabolism on all of the infants eighteen hours after the last meal, an effort was made to find out the length of time required to obtain the minimum basal metabolism after feeding milk. To this end some five or six infants were studied 1, 2½, 5, 9, 12, 18 and 21 hours after food. The difficulties in securing ideal periods of rest exactly coincident with definite periods of time after the ingestion of food are sufficiently obvious to need no special comment here; it is only necessary to state that our evidence is admittedly not so complete as we should like. A critical examination of the data shows us, however, that on the whole the influence of milk feeding on the metabolism of infants must be very slight. In certain instances the metabolism during quiet periods immediately after feeding is from 5 to 10 per cent. higher than eighteen to twenty-one hours after, while in others the metabolism twenty-one hours afterward, even in periods of complete muscular repose, was slightly greater than immediately after feeding. But the general picture derived from these observations indicates that the ingestion of milk played a very slight, if any, rôle in affecting the heat-production of the infants studied.

Recent observations in this laboratory during a thirty-one-day fast showed that as soon as food was completely withheld, the body storage of glycogen was rapidly drawn on and when exhausted, a distinct acidosis appeared. Our experience with diabetics and with normal persons subsisting on a carbohydrate-free diet[52] gives evidence that such an acidosis tends to increase the basal metabolism. Additional light has been thrown on this subject by Schlossmann and Murschhauser,[53] who have shown in a recent publication the influence of the withdrawal of food on the excretion by infants of products of acidosis, particularly acetone, diacetic acid, and beta-oxybutyric acid. Even in the first hours of fasting, definite evidence of the excretion of beta-oxybutyric acid shows the beginning of acidosis. Knowing, as we do,

51. Schlossmann: Atrophie und respiratorischer Stoffwechsel, Kassowitz Festschrift, Berlin, 1912, p. 318.

52. Benedict and Joslin: Carnegie Institution of Washington, Publication 176, 1912, p. 134.

53. Schlossmann and Murschhauser: Biochem. Ztschr., 1913, lvi, 396.

that acidosis strongly tends to increase the metabolism, one sees instantly that a point or a moment when the influence of the previously ingested food ceases and the influence of an oncoming, though slight, acidosis begins is extremely difficult, with our present knowledge, to foretell. It should not be overlooked, however, that Schlossmann and Murschhauser did not find an increased heat-production in these infants showing incipient acidosis although we are inclined to doubt the validity of drawing conclusions regarding so subtle a factor as acidosis from periods with such changes in the degree of repose.

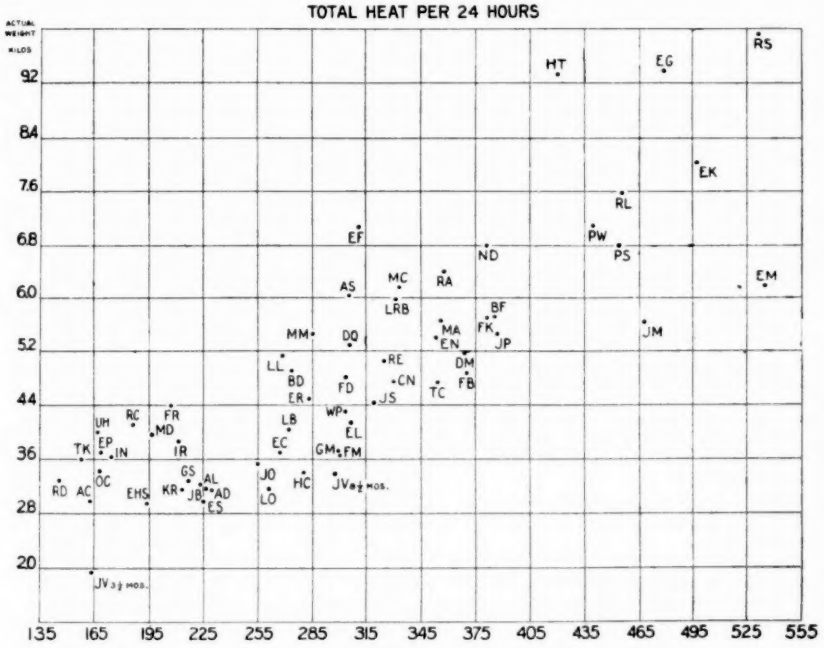

Fig. 9.—Chart showing the actual body-weight of infants and the total heat-production per twenty-four hours.

While, therefore, we recognize clearly that the presence of food in the alimentary tract of our infants has distinct theoretical objections, we believe that such influence, if it exists, can play no quantitative rôle in the striking comparisons of the basal metabolism of different infants which are made in the subsequent pages.

7. Comparison of Body-Weight and Metabolism

With the abundance of experimental material in hand, which was obtained with different infants, it is obvious that a large number of comparisons may be made in a variety of ways. Perhaps the simplest method of considering the results is on the basis of the total heat-

production. Accordingly a chart has been plotted showing the total heat-production of infants of varying weights, the actual weight at the time of the observation being used (Fig. 9). It is normally to be expected that a large animal gives off more heat than a small animal, and consequently we find that there is a tendency for the heavier infants to have a larger heat-production. Yet this is by no means invariably the case, for in a large number of instances, an infant of relatively small weight has a much larger heat-production than those of greater weight. Perhaps the most striking instance is

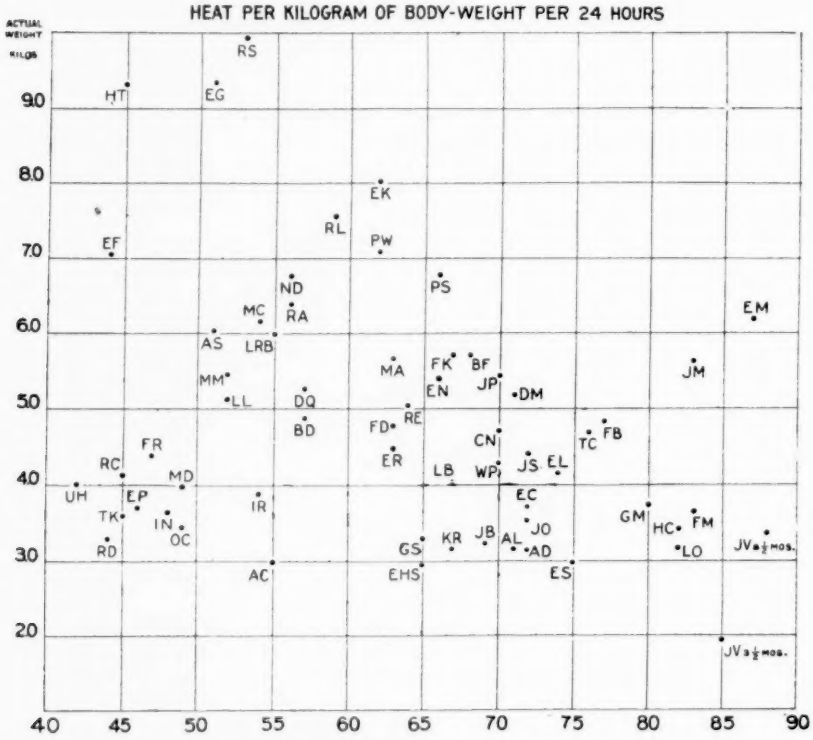

Fig. 10.—Chart showing the actual body-weight of infants and the heat-production per kilogram per twenty-four hours.

that with the subject E. M., who, with a body-weight of 6.2 kg., has 25 per cent. larger heat-production than has H. T. with a body-weight of 9.3 kg. While it is clear from the chart that in general the large infants show a larger heat-production, yet as there are many exceptions, no definite rule based solely on body-weight can be of great use. Although no general uniformity is seen at first in this curve, if one examine more particularly the values for the infants indicated as strictly normal in the table showing the clinical status of the infants

(Table 13), one can see that there is a distinct tendency to approximate a regular curve. Inasmuch as we are still occupied in overcoming the paucity of results obtained with normal infants, we hardly feel justified in laying sufficient stress on this point to designate specially the normals in our charts.

It has been the custom of many writers to compare the heat-production of persons of varying sizes by computing the heat-production per kilogram of body-weight, thus tacitly, at least, assuming a constancy in the heat-producing value of each kilogram of body-weight. Although dissenting from this principle, we have, for comparison purposes, computed the values for our infants on the basis of per kilogram of body-weight and give a part of them in Figure 10. Here there is, as would be expected, a large variation in the heat per kilogram of body-weight and no regularity is apparent. If the "normal" infants are selected, it is found that they, for the most part, lie under 65 calories per kilogram of body-weight, although they may go as low as 42 calories. For an intelligent comparison of the metabolism of different infants, therefore, it is evident that we have to deal with some factor or factors other than body-weight and no definite deduction can be drawn other than the fact that the majority of our "normal" infants have a heat-production per kilogram of body-weight somewhat under 65 calories per twenty-four hours.

8. Comparison of Body-Surface and Metabolism

For many years writers in metabolism have been wont to emphasize the significance of the relationship supposed to exist between the metabolism and the body-surface rather than that between the metabolism and the body-weight. The idea that there is an intimate relationship between body-surface and heat-production was first brought out by Bergmann[54] in 1847. The theory lay dormant for many years, but was finally resuscitated and put forth in a brilliant and highly stimulating manner by Rubner[55] in 1883, together with experimental evidence. Based fundamentally on Newton's law of cooling, it received great attention from practically all workers in physiology. The startling evidence which was brought forward to demonstrate that the heat-production per square meter of body-surface was about 1,000 calories for practically all species of animals lent further support to this hypothesis. In connection with our own researches we naturally expected to find a close relationship between body-surface and total metabolism, particularly in view of the fact that recent observations

54. Bergmann and Leuckart: Anatomisch-physiol. Uebersicht des Thierreichs, Stuttgart, 1852, p. 272. Bergmann: Wärmeökonomie der Thiere, Göttingen 1848, p. 9.

55. Rubner: Ztschr. f. Biol., 1883, xix, 545.

from foreign laboratories appeared to confirm the validity of Rubner's law. We were, therefore, greatly surprised on preparing our final figures to find this intimate relationship entirely disturbed.

A. Methods Used for Measurement of Body-Surface

In order to discuss intelligently the relationship between the metabolism and body-surface, a critical examination of the various methods for determining the body-surface is essential. Using as a basis the relationship between the surface of similar solids which is expressed by the cube-root of the square of the weight, efforts have been made by a number of investigators to compute the body-surface of various animals and persons from the body-weight.

Meeh[56] found that he could measure the body-surface of men by using the constant 12.312, which, when multiplied by the cube-root of the square of the body-weight in grams, gave the body-surface in square centimeters. Rubner and Heubner,[57] who first applied this formula to the study of the total metabolism of infants, rightly substituted the value 11.9 which was determined by Meeh on two well-nourished infants under 1 year that he measured.

Recognizing the importance of taking into consideration the length of the body as well as the circumference of breast and abdomen, Miwa and Stoeltzner,[58] using Meeh's measurements, proposed another formula in which the length and circumference as well as weight should appear as factors. This formula has not been generally accepted by research workers.

Actual measurements of the body-surface of cadavers have also been used in an attempt to find some mathematical formula expressing the relationship between body-weight and body-surface. Lissauer[59] measured twelve cadavers, eleven of which were under 1 year, and found that the constant 10.3 should be used in the Meeh formula instead of those previously proposed. It has been maintained by other writers that since many of Lissauer's measurements were made on thin, poorly nourished, and atrophic infants, they do not give standards for well-nourished infants. Sytscheff[60] measured ten infants under 1 year of age, but computed no ratios. Howland,[43] employing Meeh's and Lissauer's measurements, has recently proposed still another method for computing the body-surface based on a curve represented by the algebraic formula $y = mx + b$.

56. Meeh: Ztschr. f. Biol., 1879, xv, 425.
57. Rubner and Heubner: Ztschr. f. exp. Pathol. u. Therap., 1904-1905, i, 1.
58. Miwa and Stoeltzner: Ztschr. f. Biol., 1898, xxxvi, 314.
59. Lissauer: Jahrb. f. Kinderh., 1902, lviii, 392.
60. Sytscheff: Measure of Volume and Body-Surface of Children According to Their Ages. Dissertation, St. Petersburg, 1902. See also Gundobin, loc. cit., p. 54.

With these three methods in vogue for computing the body-surface, that is, that of Rubner and Heubner using the Meeh formula with the constant 11.9; that of Lissauer using the constant 10.3 and that of Howland using the algebraic curve, it can be seen that with the great weight laid by all experimenters in infant metabolism on the relationship between body-surface and metabolism, it is incumbent on us to present our results on the three separate bases, although the relative values are unaltered in all three cases. This is done in Table 15.

B. Comparison of Actual Body-Weight and Heat-Production per Square Meter of Body-Surface

According to accepted ideas we should expect the heat-production per square meter of body-surface to be approximately constant for all of our infants. That this fact is far from being true is clearly

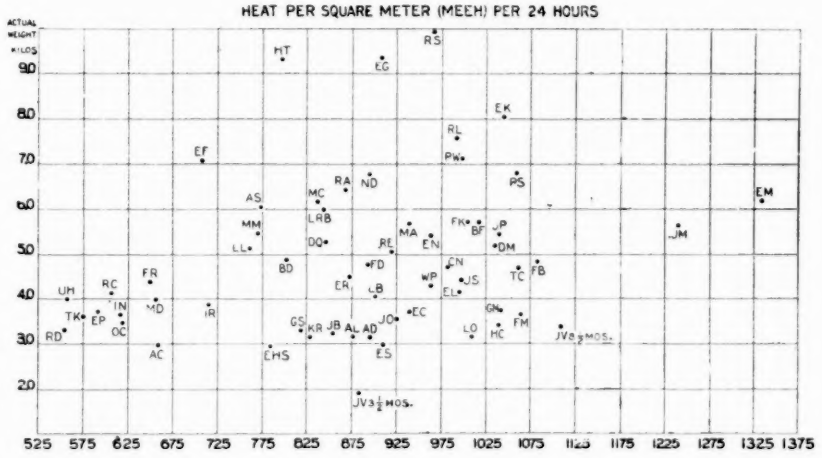

Fig. 11.—Chart showing actual body-weight of infants and heat-production per square meter of body-surface (Meeh formula) per twenty-four hours.

seen in Table 15, but the variations are most strikingly shown if we compare them with the actual body-weight of the infant, as is done in Figure 11. In this chart, which is made up on the Meeh formula, we should expect to find the values grouping themselves in a vertical line. On the contrary, the dispersion of the values is very noticeable, with a tendency, if any, toward a horizontal rather than a vertical alignment. An actual variation from 554 to 1,334 calories or 140 per cent. is recorded. Omitting the extreme cases, J. M. and E. M., although frankly we see no reason why they should be omitted in this comparison, the range is 554 to 1,108 or 100 per cent. Even "normal"

infants range from 554 to 998 calories. Thus the complete absence of correlation between weight and the heat-production per square meter of body-surface is strikingly shown. It is again important at this point to recall the fact that the observations made on these infants were all under constant conditions, namely, complete muscular repose and approximately the same length of time after feeding. It is impossible, therefore, to explain these great discrepancies as due to muscular activity, nor can they in any way be accounted for by the ingestion of food, as our experiments have shown that the food taken by these infants while under observation has no material influence on the metabolism. Although we are deferring its discussion until a later article, it is of interest to point out here the low heat-production per square meter of the numerous new-born infants.

9. Effect on Metabolism of Possible Disturbance in Relationship Between Body-Surface and Body-Weight

It has frequently been the custom when discrepancies in the heat-production per square meter of body-surface are found with infants, and particularly with atrophic infants, to ascribe the variation to a disturbance of the relationship between body-surface and the body-weight from which it is computed. It is essential, therefore, at this point to discuss this possibility more in detail.

The argument frequently raised is that disturbances in the relationship between body-weight and body-surface with underweight infants precludes the use of any of the formulas now regularly used for the computing of body-surface, in that they give too small a value of body-surface for such infants. At the outset we wish to oppose this general thesis on the ground that in the most extensive and remarkably accurate series of measurements on infants with which we are familiar, namely, those of Lissauer, it is especially emphasized that ten out of twelve of the infants were very much under weight. This will be seen by reference to Table 16, which reproduces the weights of eleven of the infants measured by this investigator.[59]

As Lissauer himself points out with regret, S-i was the only infant that could be called normal, although S-r was practically of normal weight. All of the other infants were noticeably under weight, far more so than our infants as a rule. Yet, in spite of this great deficiency in weight, the relationship between the body-weight and the measured body-surface was represented by the difference between the constant 10.3 used by Lissauer and 11.9, the constant of Meeh. In other words, this large variation in weight produced a maximum discrepancy of not over 15 per cent. in the relationship between the body-surface as actually measured and the body-weight.

We believe that Lissauer's formula, in general, more nearly fits the requirements of observations in clinics, where the larger number of infants are under weight. On the other hand, as we have already pointed out, it is distinctly questionable whether the methods of measurement[61] have even yet been sufficiently refined or are sufficiently numerous to give a reliable method for the computation of the body-surface from the body-weight.

Although we believe that the lack of consistency exhibited by our infants in the heat-production per square meter of body-surface may not be ascribed to the fact that these infants were distinctly under the

TABLE 16.—Body-Weights of Infants Measured for Body-Surface by Lissauer

Name	Sex	Age	Body-Weight, kg.	Average Weight for Age Obtained from Heubner, kg.
M-f.....	M	3½ months	3.27	6.2
H-r.....	F	3½ months	1.96	6.2
R-e.....	F	3¾ months	3.37	6.3
S-e.....	M	1 month	2.22	4.008
S-r.....	F	1 month	3.83	4.008
M-r.....	M	15 months	5.23	11.+
W-t.....	M	17 days	1.73	3.6
S-t.....	M	22 days	1.28	3.7
P-z.....	M	3¼ months	2.50	6.0
H-z.....	M	7½ months	3.10	8.2
S-i.....	M	3⅔ months	6.18	6.3

average weight, it is of special interest to select a few infants who are of normal average weight and note the relationship between the heat-production and the body-surface. This has been done in Table 17, in which the heat-production per square meter has been calculated for eight of our normal infants of average weight.

61. As an interesting evidence of our initial belief in the importance and significance of the measurement of body-surface and its relationship to metabolism, we should here state that extensive preparations were made by us for the measurement of the body-surface of a number of infants, and a method was developed for securing shadow photographs of infants in various positions, the areas of the shadows being measured by a planimeter. It was our hope to establish thereby some relationship with the body-surface as measured from the shadow photograph, and by actual measurements of cadavers, and the body-weight and length. It is needless to say that with our present views in regard to the significance of body-surface in the relation to metabolism we have not felt justified in continuing such a series of measurements.

10. *Influence of Variations in the Composition of the Body on Total Heat-Production*

Since a gross disturbance in the relationship between the body-weight and the body-surface as computed from the body-weight is highly improbable whether the infant is atrophic or well-nourished, it is important to find out, if possible, if any relationship exists between the general composition of the body and the total heat-production. Our data are sufficiently extended to permit a somewhat incomplete discussion of this important phase of the comparisons.

Heretofore, all workers in metabolism have considered only the relationship between body-weight and metabolism, or body-surface and metabolism. Since the body-surface is assumed to have a direct relationship to the body-weight, it can be seen that body-weight is

TABLE 17.—HEAT-PRODUCTION PER SQUARE METER OF BODY-SURFACE (MEEH FORMULA) FOR NORMAL INFANTS

Subject	Body-Weight Without Clothing kg.	Height cm.	Age	Experimental Days	Periods	Heat per Square Meter of Body-Surface (Meeh) cals.
M. D.	3.99	..	17 days	2	4	656
L. L.	5.13	57	2½ mos.	10	13	759
B. D.	4.90	58	2 mos.	2	4	802
M. C.	6.17	63	4 mos.	3	7	837
L. R. B. ..	5.99	64	4 mos.	4	11	844
E. G.	9.37	74	10 mos.	3	5	907
R. L.	7.58	71	8½ mos.	5	8	991
P. W.	7.11	64 ?	7 mos.	2	5	998

the only fundamental factor which has thus far been seriously considered by investigators in comparing the metabolism of different infants.

It is obvious that when two infants are of the same weight, the shorter one will have the larger proportion of fat. Furthermore, with two infants of the same length but of different weights, the heavier infant will have the larger proportion of fat. It can be seen, therefore, than an atrophic infant, weighing 4 kg. and 65 cm. long, when compared to a well-nourished infant of the same weight and length, would have a smaller proportion of fat. Moreover, an atrophic infant, to have the same weight and length as a normal infant, must obviously be older, and we here find a new factor entering into the comparison of infants; as yet the element of age has received scant attention.

An inspection of Table 15 will show that in a number of instances infants with approximately the same body-weight and the same height differ greatly in age. Unfortunately our data are not so extensive as to enable us to compare infants with absolutely the same body-weight and height, but a number of comparisons are justifiable and these have been included in Table 18.

In this table eight series of comparisons are made of the total heat produced, the heat-production per kilogram of body-weight, and the heat-production per square meter of body-surface for infants with

TABLE 18.—COMPARISON OF HEAT-PRODUCTION OF INFANTS OF LIKE BODY-WEIGHT AND HEIGHT, BUT OF DIFFERENT AGES

Subject	Sex	Body-Weight kg.	Height cm.	Age mos.	Heat Produced		
					Per 24 Hours cals.	Per Kilogram per 24 Hrs. cals.	Per Sq. Meter (Meeh) per 24 Hrs., cals.
A. L.....	F.	3.18	53	4	226	71	876
J. V.....	F.	3.38	53	8½	297	88	1,108
E. N.....	F.	5.40	66	6	353	66	962
D. M.....	M.	5.18	66	11	369	71	1,034
M. M.....	F.	5.47	62	4½	285	52	770
J. M.....	M.	5.63	62	8	467	83	1,239
D. Q.....	M.	5.28	62	4½	305	57	846
J. P.....	M.	5.45	63	7	387	70	1,039
M. M.....	F.	5.47	62	4½	285	52	770
J. P.....	M.	5.45	63	7	387	70	1,039
D. Q.....	M.	5.28	62	4½	305	57	846
J. M.....	M.	5.63	62	8	467	83	1,239
L. R. B.....	F.	5.99	64	4	331	55	844
F. K.....	M.	5.71	65	7	381	67	1,003
H. T.....	M.	9.33	75 ?	5½	420	45	797
E. G.....	M.	9.37	74	10	479	51	907

the same body-weight and height but of different ages. The difficulties incidental to measuring exactly the length of infants make these measurements slightly problematical and there may be a variation of plus or minus 1 cm. We have, therefore, compared infants whose lengths do not vary more than 1 cm. The variations in weight are all within a few tenths of a kilogram.

We note instantly several striking points in the data as presented. In each comparison the values for the younger infant are given first,

and it will be seen that the older infant has invariably the larger total heat-production. The greatest difference is 182 calories in the comparison of M. M. with J. M., the lowest difference being that of 16 calories between E. N. and D. M. Aside from this latter comparison, the increase in the heat-production for the older infants is very considerable. The heat-production per kilogram of body-weight and per square meter of body-surface also shows this increase in the same general proportion since the body-weights of the infants compared are essentially the same in all cases.

In the two series of comparisons in which the youngest infant is approximately 6 months old, namely, those comparing E. N. with D. M. and H. T. with E. G., the increase in the heat-production for the older infant is not so great. In the latter comparison, E. G. was of normal weight while H. T. was over weight so that the excessive amount of fat actually lowered the total heat-production of the younger infant H. T. It is therefore clear that with the older infants, which were in most instances distinctly under weight, there was a deficiency in the fat with an accompanying increase in the proportion of active protoplasmic tissue. While this method of comparing the metabolism of infants on the basis of weight, height and age gives a clue to the probable preponderance of fat or active protoplasmic tissue, it is obvious that no quantitative relationship can be established on this basis.

The striking comparison between M. M. and J. M. is particularly worthy of consideration, inasmuch as the value for M. M. is derived from observations on three days, and a total of seven satisfactory periods were available for averaging, while with J. M. the data were secured on two days with six periods for comparison. Here, with a difference of 3½ months in the age, there was obviously a much greater proportion of active protoplasmic tissue with the older infant, J. M.

That the active protoplasmic tissue determined to a very considerable extent the total catabolism, not only with J. M., but with all of the older undernourished infants, is highly probable and we find ourselves thoroughly convinced that the metabolism is determined not by the body-surface but by the active mass of protoplasmic tissue. With normal infants of varying weights, it is quite probable that the active mass of protoplasmic tissue varies directly with the age. Since it has been shown that not only body-surface but also more recently the blood-volume, the size of the aorta, and the size of the trachea with several species of mammals bear a direct relationship to the cube root of the square of the body-weight,[62] it is not surprising that most

62. Dreyer and Ray: Phil. Tr., 1909-1910, cci, ser. B, 133; Dreyer, Ray and Walker: Proc. Roy. Soc., London, 1912-1913, lxxxvi, ser. B, 39 and 56.

experimenters have observed that with adults the metabolism is roughly proportional to the body-surface. If the blood-volume and the area of the trachea and the aorta are proportional to the cube root of the square of the body-weight, it is reasonable to suppose that the active mass of protoplasmic tissue may develop normally on this ratio. When there are marked variations from the average, as with excessive or with deficient adipose tissue, this relationship cannot be expected to hold.

If, therefore, it is maintained that the total metabolism is proportional to the body-surface, it should be stated that this is not due to the fact that there is a loss of heat from the body-surface and that Newton's law of cooling determines the intensity of the metabolism, but that with normal persons the body-surface, blood-volume, the area of the trachea and aorta, and probably the active mass of protoplasmic tissue, are all in simple mathematical relation to the body-weight. Thus the apparent relationship which has previously been observed between the heat-output and the body-surface with normal or nearly normal persons has an explanation in that with such persons a simple relation exists between the body-surface, blood-volume, body-weight, and the mass of active protoplasmic tissue.

In our series of observations we have attempted to eliminate completely all muscular activity, to make the experiments under approximately the same conditions as to nutriment, to select such a diet as was least stimulating to the catabolism and to have our subject for the most part in deep sleep, thus eliminating psychic disturbances. With these conditions we hoped to obtain the fundamental minimum metabolism, on which we might base our discussion.

The basal metabolism as we have outlined above, cannot in any wise be considered a direct function of the body-weight and the body-surface and particularly has no relationship with body-surface on the basis of the law of cooling bodies.

We believe that our evidence points strongly and conclusively to the fact that the active mass of protoplasmic tissue determines the fundamental metabolism. The absence as yet of a direct mathematical measure of the proportion of active protoplasmic tissue does not, we believe, in any wise affect the convincing nature of our evidence.

A CASE OF ACUTE CHYLOUS ASCITES (NON-FATTY, PSEUDOCHYLOUS, LACTESCENT OR MILKY TYPE) IN A BOY EIGHT YEARS OLD*

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OPERATIONS AND SURGICAL COMMENTS BY
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In a recent most valuable, thoroughly scientific and exhaustive monograph Dr. S. Gandin of St. Petersburg, discusses the different types of chylous effusions in serous cavities. The work is based on the study of three medical and two surgical cases, and a critical review of 281 references covering the literature up to date.

The classification chylous, chyliform and milky, non-fatty forms of ascites, is not universally adopted. Many of the more recent writers make no distinction between the chylous and chyliform varieties; others prefer to retain the designation chyliform (which does not necessarily refer to the origin of the fluid), some again do not make any distinction between the fatty and the non-fatty ascites, regarding them, in contradistinction to the chylous, as chyliform or pseudochylous.

This confusion has led to a further distinction of mixed types, chylous-adipose, chylous-pseudochylous and adipose pseudochylous effusions.

1. The *true chylous* is due to the presence of chyle. 2. The *chyliform or fatty*, though resembling the first, owes its milky-like appearance to emulsified fat, the result of a fatty degeneration of cellular elements. 3. Finally, in the third variety, the opalescence is not due to the presence of fatty emulsion, but is caused by some opalescent substance, the exact nature of which is still undiscovered.

Chylous ascites is due to the escape of chyle from the duct or receptaculum chyli, the result of trauma or disease processes, malignant or benign. The specific gravity varies from 1.007 to 1.033, average 1.0158. The reaction is alkaline or neutral.

The fluid resists putrefaction, is without odor, does not clot, but may separate into layers on standing, the fat appearing on top. This variety is distinguished, first, by the finely divided state of the fat, and

* Read by title at meeting of the American Pediatric Society, May, 1914.

secondly, by the absence of leukocytes or other cells showing fatty changes.

The chylous and chyliform effusions have been carefully studied, not only as to their composition, but also from the pathological standpoint. Wallis and Scholberg (1910) believe that there are no characteristic pathological anatomical changes.

Kelly (1907) would restrict the name to cases in which injuries or ulcerations of the chylous system have been found.

Witlin (1909) believes that chylous ascites or chylothorax can only be explained by trauma.

Between these extremes there are those who would explain the occurrence by stasis or evidence of pressure on the thoracic duct; others find macroscopic changes somewhere in the chylous system; finally some base their diagnosis on microscopic changes in the vessels, or on the grounds of an individual anatomical predisposition.

Undoubted cases of a rupture (trauma or result of disease processes) in some portion of the chylous system, have been reported as of occasional occurrence.

Mechanical obstructions in any part of the course of the duct from the receptaculum chyli to the left subclavian vein, or in some of the tributaries in the mesentery, the result of cicatricial contractions, new growths, cysts or tumors, may give rise to stasis and transudation through the weakened and dilated walls. In some of these cases diffuse dilatations of the main duct or entire chylous system were found; in others more or less localized distention of the vessels in the mesentery and intestinal walls existed, depending on the situation of this obstruction. It must be remembered that pathological conditions which lead to a gradual interference in the ductus are more readily compensated through the collateral circulation than those of acute origin, a circumstance which may explain the rarity of cases.

Chyliform or fatty (adipose) ascites differs from the above. It is not due to leakage of chyle but to the formation of fat in the effusion; the globules are larger and cells containing fat are present, specific gravity 1.009 to 1.026; average, 1.01625. It is usually associated with intra-abdominal new growths or with chronic peritonitis, simple or tuberculous.

The origin of the fatty, lactescent type, has been attributed to fatty degeneration of cellular elements, a lipemia, etc.

The non-fatty, pseudochylous, lactescent or milky type is differentiated, as the name implies, by the absence of fat. Specific gravity 1.005 to 1.030; average, 1.0132.

1. Such an effusion does not lose its milky appearance after being shaken up with ether, benzol, chloroform, etc., even though rendered alkaline beforehand.

2. When fat is present the amount is too small to give rise to a milky appearance.

3. The microchemical reactions of fat (specific color, effects of heat and fat solvents) are negative.

4. Precipitation of the albumen leaves a clear solution.

5. Finally in a number of cases the opalescence is presumed to be due to minute particles of albumen, nucleo albumen, mucoid, lecithin, lecithoglobulin, etc. Gandin,[1] who has carefully reviewed the voluminous literature and weighed the evidence, does not believe that the negative results of the microchemical reaction of the so-called pseudochylous fluid invalidate the assumption of the fatty nature of suspended molecular granules.

In considering critically and at length the various properties (physical, microscopic, chemical, and physiological) of chylous, chyliform and pseudochylous fluids, Gandin[1] is unable to establish any important differential characteristics; furthermore, he does not think that we are justified in the use of the above-mentioned classification. A thorough critical review of the pathogenesis of the chylous and pseudochylous types leads to a similar result. His conclusions based on his studies and experiments, are briefly as follows:

GANDIN'S CONCLUSIONS

1. The addition of even small percentages (0.01 to 0.1 per cent.) of the finely emulsified fat of chyme or homogeneous milk to a transparent fluid gives rise to a milky cloudiness.

2. The milky appearance of an effusion in a serous sac is due to the presence of emulsified fat.

3. It has not been demonstrated in a satisfactory manner, that the presence of any substance excepting emulsified fat, can give rise to the milky appearance. The presence of emulsified fat in milky effusions, without the admixture of chyle is not probable, nor has such been demonstrated.

4. As chyle represents the only recognized source of finely emulsified fat in the body, milky and opalescent effusions must be regarded as chylous.

5. The terms "chyliform" and "pseudochylous" are not applicable as distinct pathogenetic entities, consequently they are superfluous.

6. Effusions, containing fat in drops, but not in an emulsified form, do not present the typical milky appearance.

The term fatty (adipose), introduced by Quincke, is applicable to such cases.

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1. Gandin, S.: Patogenese und Klassification der Milchartigen Ergüsse, Ergebn. d. inn. Med. u. Kinderh., 1913, xii, 219.

CASE REPORT

History.—S. H., male, aged 8, was admitted to Beth Israel Hospital Dec. 15, 1913. He was born in New York and had never been in any of the southern or eastern countries.

The family history has no bearing on the case. He had measles when 7 months old, and what was supposed to have been a nephritis, with edema of the extremities, clearing up after four weeks illness, at age of 4 years. With the exception of pneumonia at 5½ years, the boy was reported to have enjoyed fair health up to the time of his present illness.

Careful questioning failed to elicit any history of trauma. Two weeks before admission the child felt generally ill, suffering from a severe nasal discharge, though he continued to attend school. A week later he vomited undigested food, since which time his appetite has been poor. Two days before he entered the hospital the father on dressing the child noticed an increase in the size of the abdomen and a swelling of the genitals. No fever, cough, headache, general weakness or urinary disturbances were present.

Physical Findings.—The patient was fairly well developed, somewhat anemic and rather poorly nourished. No evidences of prostration, dyspnea, no petechia or other eruption or glandular enlargement were noticed.

Heart and lungs negative. Abdomen symmetrically enlarged, fluctuation wave readily transmitted from side to side. Careful palpation failed to reveal a tumor or any swelling in the abdominal cavity; no tenderness or rigidity present. The veins were markedly distended over the lower half of the abdomen and right upper quadrant; also over the upper parts of both thighs. The center of the abdomen was tympanitic; the flatness in the flanks, changing quickly with a change in the position of the patient, showed a large amount of free fluid in the abdominal cavity.

The edema of the penis and scrotum was quite marked. There was slight edema of the thighs, but none about the feet or ankles; abdominal walls and back slightly infiltrated. The temperature was 100 F. It quickly fell to normal and remained so. The pulse, which was 120, rapidly came down to 80, varying between 80 and 100; at times 110. The respirations were 24 to 30. Red blood-cells, 4,700,000; hemoglobin, 70 per cent.; white blood-cells, 9,800; lymphocytes, 16 per cent.; polynuclears, 79 per cent.; eosinophils, 4 per cent.; mastcells, 1 per cent; urine negative. Von Pirquet negative on repeated occasions. Wasserman also negative.

Two weeks later red blood-cells, 3,500,000; hemoglobin, 65 per cent.; white blood-cells, 10,000; lymphocytes, 11 per cent; polynuclears, 88 per cent.; eosinophils, 1 per cent. Phenolsulphonephthalein test for renal efficiency 30 per cent. on one occasion and 20 per cent. the second.

Though the general condition remained excellent, appetite "simply enormous" with regular bowels, the abdomen became larger, the diaphragm being pushed up as high as the middle of the scapula on the right side, and lower angle on the left. Edema of the genitals and thighs, particularly the left, also increased; the subcutaneous tissues of back and abdominal walls pitted on pressure. Notwithstanding distention there was relative little discomfort or dyspnea. The urinary excretion was greatly diminished, about 8 or 9 ounces daily, though allowed at least 20 ounces of fluids. Urine negative, no casts, cells or bacteria.

Management.—Jan. 6, 1914, the abdomen was tapped in customary manner; over 3,000 c.c. of a slightly turbid, milky fluid were removed to relieve the distention. A considerable amount, approximately half, was allowed to remain. Microscopically a few lymphocytes and some finely granular matter with brownian movements were found. Evaporating a drop on the slide, crystals of sodium chlorid were detected. A bacteriological examination failed to reveal any organisms. No sugar or fat present.

EXAMINATION OF ASCITIC FLUID

From S. H.

Quantity about 500 c.c.; color and appearance, milky, still turbid after filtration; specific gravity, 1.011 (20 C.); reaction, neutral; total solids, 1.25 per cent.; material in suspension, 0.016 per cent.; ash, 0.72 per cent.; organic matter, 0.53 per cent.; sodium chlorid, 0.64 per cent.; sulphates, *nil;* urea, *nil;* sugar, *nil;* albumin, 0.319 per cent.; primary proteose, 0.055 per cent; secondary, also present, unestimated; globulins (indications ?) not estimated; fats, absent.

LOUIS E. SALAS, M.A., B.Sc.

For four or five days subsequently, considerable oozing took place through the small puncture, necessitating a change of dressing several times daily. The edema of the scrotum and abdominal walls diminished. As soon as the slight wound had healed, the abdomen refilled rapidly and the edema of the back, abdomen and thighs also increased, necessitating a second tapping. January 17 over 2,000 c.c. were taken away. It presented the same opalescent appearance, similar to that removed before. The rapid recurrence of the ascites, it seemed to us, demanded more radical measures. If the abdominal fluid, rich in proteins, salts, and the characteristic constituents of the tissues and body fluids could be diverted to the blood and lymph streams, the patient certainly would gain in every way. After a consultation with my surgical colleague, Dr. H. M. Silver, an exploratory laparotomy was decided on, first, with a view to a clearing up the nature of the lesion, and secondly, to determine the possibility of draining the "peritoneal pond" into the subcutaneous tissues of the thighs and abdominal walls. This part of the subject will be taken up by Dr. Silver to whom my sincere thanks are tendered for his interest and skilled surgical aid in the care of this interesting case.

Diagnosis.—A careful consideration of the physical condition and the history of our patient did not enable us to hazard any suspicion as to the etiology. In the absence of any traumatism, the rapid appearance of ascites, the large prominent veins with local edema of abdomen and genitals, pointed to some intra-abdominal pressure, though no tumor or other swelling could be detected, even after tapping. The general appearance and bearing of the child were against malignancy.

The character of the fluid obtained by tapping, its milky opalescent hue, and the absence of cells filled with fat, justifies a diagnosis of chylous ascites (third variety), non-traumatic in nature and of uncertain origin.

DISCUSSION

A majority of the writers believe that the chylous origin of the fluid may be established or recognized clinically, first, by the "test of Strauss"; secondly, by the rapid return of the fluid after tapping.

The Strauss test is based on the fact that the amount of fat in the chyle depends on the diet. Thus, if a larger amount of fat is allowed or a smaller percentage is taken in, corresponding changes will be noticed in the fat contents of the fluid removed in repeated tappings at regular intervals. Though confirmed by some, the results obtained by other observers have been rather conflicting.

The rapid accumulation of the fluid noted in our case and in others reported in literature, has been the subject of comment by many authorities.

It was observed by Vermage in 1700, and confirmed by many writers subsequently.

Senator attributes the rapid recurrence to stasis, either in the portal system or in the chyle-duct or lymphatic circulation. Others conclude that there has been a rupture of some portion of the duct or one of the tributaries, permitting the escape of chyle into one or other of the serous cavities. On the other hand, instances have been recorded in which the fluid did not return quickly. And furthermore we should not forget that in other pathological states, as advanced cases of cirrhosis of the liver, in which the question of chylous ascites does not enter, a rapid return of the fluid is not unusual.

Aside from the presence of the chylous fluid, the case is interesting in many other respects. For instance:

1. The small amount of urine passed. Though only 8 or 9 ounces were excreted in twenty-four hours, there was no evidence of any systemic disturbances, as headache, nausea, vomiting, etc.

2. The general well being of the patient. Excepting the discomfort due to the distended abdomen, the boy did not make any complaint. The appetite was good and bowels regular. Pulse and temperature normal.

3. The rather unusual type of ascites with edema of the back, abdomen, thighs and genitals (ankles, legs and chest, not involved) and no edema of the face at any time throughout the course of the disease.

4. The rapid return of the fluid after tapping, presumably explained by the fact that a collateral circulation had not been established, as condition was rather acute.

5. The marked diminution in the amount of edema of abdomen, genitals, etc., after the tapping, and its rapid return when the puncture had healed.

6. The rapid subsidence of the external localized edema after operation.

7. The decided increase in the urinary excretion soon after operation, evidently the direct results of the removal of the intra-abdominal pressure and the establishment of peritoneal drainage.

8. The brilliant success of the surgical measure adopted.

OPERATION WITH SURGICAL NOTES

HENRY MANN SILVER, M.D.

Early in January of this year (1914) Dr. F. Huber requested me to see and operate on a boy 8 years old, suffering from chylous ascites. As a careful history of the case has been given above, it will not be necessary to repeat it. Although the patient was in rather poor condition, and the fact was recognized that ascites patients have an impaired vital resistance, deficient powers of repair, and do not stand

well extensive operations under general anesthesia, it was decided to do an exploratory laparotomy as quickly as possible under ether anesthesia.

Exploratory Laparotomy.—An incision beginning just below the umbilicus and extending downwards for 3 inches just to the right of the median line was made through the layers of the abdominal wall. When the peritoneum was opened considerable fluid escaped and about 1,500 c.c. were drawn off by the aid of the suction apparatus.

The coils of small intestines presenting in the wound were greatly distended with gas and very pale, and on careful examinattion of all the coils within reach a most interesting condition was observed. The lacteal vessels, not only on the intestines, but in the mesentery, were much enlarged, being flexuous in their course, constricted at intervals and presenting a beaded or varicose appearance. The constrictions on the intestines were so tight in places that the lacteal vessels would disappear only to reappear in the mesentery. Enlarged glands were found in the mesentery, small near the intestines, but growing larger as they passed to the root of the mesentery where they became very numerous. Some were about the size of a small hickory nut, soft, elastic and of a yellowish color. It was not deemed advisable to remove one for the purpose of closer study and microscopic examination, as the child's condition was not good. As careful an examination was made of the organs within the abdominal cavity as was possible through a 3-inch incision. Nothing abnormal was detected. Before closing the wound, the question of what form of drainage should be resorted to, presented itself.

The ascites was chylous, came on quietly, the child had not been living with any tuberculous patient at home, gave no history of injury, and there were no evidences of compression of the portal vein, as the intestines and omentum were pale and showed no sign of congestion. As it seemed to me that the ascites was due to compression and distention of the lymphatic or chylous vessels by the large number of enlarged glands within the mesentery, some simple form of internal drainage which could be quickly done was called for. This would relieve the intra-abdominal pressure until the child's general condition could be improved by good food, fresh air, sunlight and possibly some form of medication. Moreover, it would conserve a fluid rich in proteins, salts and the characteristic constituents of the body fluids; the little boy had already lost over 5,000 c.c. of this fluid withdrawn at two previous tappings.

The internal drainage was carried out as follows: Six strands of No. 7 white silk 4 inches long were caught in the grasp of a narrow-bladed dressing forceps, carried into the abdomen and thrust through the peritoneum to the outer side of the femoral vessels into subcutaneous tissues of the thigh, only half an inch of the silk remaining within the peritoneal cavity. This was repeated on the opposite side. At the upper angle of the wound six more strands of silk of the same length as used below were thrust into the subcutaneous tissues of the abdominal wall above the umbilicus, the lower half inch remaining within the abdominal cavity. Great care was taken to allow only a very little of the silk to project within the abdominal cavity, as it has been found by actual experiment that long silk strands may cause intestinal obstruction by forming attachments to the omentum or any organ within reach.

Course.—The patient reacted well and his convalescence was rapid and uneventful. The dressings were removed at the end of a week and the wound was found completely healed, with no edema of its edges. There was some edema in the upper part of the right thigh, very litttle in the left thigh, and none over the upper portion of the abdomen. The patient was allowed to be up and about the ward early in order to maintain the circulation of the body fluids by exercise, especially in the portal and lymphatic systems. The boy was discharged from the hospital in fine condition the latter part of March.

No evidences of fluid within the abdomen could be found; there was no edema of the thighs or abdominal wall; no thickening of or about the silk drains could be felt.

Five months after operation the boy was found to be in excellent health; the fluid had not returned. Abdomen lax, no masses could be felt on a most careful examination, nor could any thickening be made out in the neighborhood of the silk drains.

Although Lambotte[2] of Antwerp, was the first to use silk to drain the abdomen, it was not until Mr. W. Sampson Handley[3] published his work on the use of silk for artificial lymphatics in cases of brawny arm in the last stages of breast cancer, also its use in draining fluid from the abdominal cavity, that surgeons began to give this method of drainage any attention. Handley from an experience gained from an interesting case of ascites which showed but little edema of thighs and upper abdominal wall after operation, draws the following inferences:

(1) Without causing edema, drainage into the thigh has gone on since the operation; (2) if the absorptive powers of the tissues are normal, and the amount of fluid led into them is not excessive, the appearance of edema is not to be expected.

McDill[4] in order to determine the exact changes that took place in the silk used for abdominal drainage carried on a number of experiments in animals. He found that the short intra-abdominal ends showed a densely organized membrane of connective tissue outside of the silk and a general infiltration of the meshes by cells, single, in bundles, and in septa; although the angle of the silk with the peritoneum is plainly marked, showing an actual ectropium of the peritoneum along side of the silk which really acts as a silk connective tissue plug. This angle is the place at which McDill claims that an intraperitoneal fluid must find its exit by pressure and gravity to the subcutaneous lymph spaces, along the outside of and not within the body of the silk.

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2. Lambotte, E.: Semaine méd., 1905, xxv, 19.
3. Handley, W. S.: Brit. Med. Jour., April 16, 1910, p. 925.
4. McDill, J. R.: Surg., Gynec. and Obst., Nov., 1913, p. 523.

PROGRESS IN PEDIATRICS

REVIEW OF THE LITERATURE ON THE FEEDING AND GASTRO-INTESTINAL DISEASES OF INFANTS, FOR THE YEAR 1913-1914

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CHICAGO

BREAST-FEEDING

1. Kleinschmidt: Monatschr. f. Kinderh., 1913, xii, 423.
2. Czerny: Med. Klin., 1913, ix, 895.
3. Langstein: Ztschr. f. Kinderh., 1913, vii, 193.
4. Ritter: (Abstr.) Jahrb. f. Kinderh., 1913, lxxviii, 613.
5. Frost: Arch. Pediat., 1913, xxx, 608.
6. Reuben: Arch. Pediat., 1914, xxxi, 176.
7. Bamberg: Ztschr. f. Kinderh., 1913, vi, 424.
8. Langstein: Jahreskurs. f. Aerztl. Fortbild., 1912, iii, No. 6.
9. Koller: Cor.-Bl. f. schweiz. Aerzte, 1912, xlii, 777.
10. Rosenstern: Deutsch. med. Wchnschr., 1912, xxxviii, 1834.
11. Jones': Arch. Pediat., 1914, xxxi, 24.
12. Hoobler: Arch. Pediat., 1914, xxxi, 171.
13. Talbot: Boston Med. and Surg. Jour., 1913, clxix, 760.
14. Lee: Arch. Pediat., 1913, xxx, 509.
15. Engel: Monatsch. f. Kinderh., 1913, xii, 559.
16. Heydolph: Jahrb. f. Kinderh., 1913, lxxviii, 216.

In all recent publications on infant-feeding the superiority of breast-milk over all artificial foods is more than ever emphasized; and the crusade for the encouragement of breast-feeding continues. The cause of this undoubted superiority is still an unsolved problem. One especial phase of the subject which is greatly discussed is the far greater immunity to infection shown by breast-fed infants. This is emphasized by Kleinschmidt,[1] Czerny,[2] Langstein,[3] Meyer and others. They have shown that all methods of artificial feeding, however successful in other respects, give no immunity against infectious processes. What is the essential cause of the high immunity conferred by breast-milk? The passage of immune bodies from mother to infant in the mother's milk has long been considered a possibility. Czerny[2] believes that this has not been proved; but believes the cause lies rather in the high fat content of breast-milk. Langstein[3] advises feeding all infants who are much exposed to infection on breast-milk.

A theory advocated for some time by German authors is that there is shown but little variation in the breast-milk of different women, or in the same woman under different conditions; that all breast-milk is

good. Langstein says that differences in breast-milk have not been proved; that until they are he will adhere to the idea that all breast-milk is adapted to the child.

Bamberg[7] studied the composition of the milk of wet-nurses giving very large amounts of milk; also of a few during menstruation. He found no change in the constituents under these two conditions.

Heydolph[16] saw no bad effects in infants after continuance of breast-feeding during mastitis, even though there was pus in the milk.

Ritter,[4] on the other hand, believes that all breast-milk is not alike, and that the wide variations in fat should be studied. Frost[5] believes that nervous shock in the mother may cause changes in the breast-milk harmful to the infant, and that under such circumstances all the constituents of the milk may be changed.

Reuben,[6] in a large experience at milk stations, finds that the breast-milk of most of the women deteriorates or becomes insufficient after the seventh or eighth month; and that the children weaned altogether at that time thrive much better than those given *"allaitement mixte."* Langstein, too, on the ground that after the ninth month the breast-milk contains too little iron, advises weaning and the giving of a small amount of vegetable purée, besides the feedings of milk dilutions.

Jones[11] has reviewed the recent statistics as to the ability of mothers to nurse their infants.

Most authors seem agreed that the only stimulus for milk secretion is the normal one of the sucking of the infant; so that in the event of a delayed or insufficient milk secretion, waiting, with a systematic putting of the infant to the breast, are indicated.

Koller[9] disagrees; he believes that milk secretion is not merely passive, caused by suction on the nipple, but active, depending on the nervous condition of the mother. Rosenstern[10] has shown that in many cases of apparently insufficient milk-supply the fault was in the failure of the infant to suck properly. These cases usually would have been considered cases of insufficient secretion of the mothers; that this was not true was proved by the fact that all the mothers were able to pump off considerable amounts of milk after each feeding. The cases observed were for the most part in very young infants, and the cause he suggests is that previously brought forward by Finkelstein: the possibility of the late development of the sucking reflex in these infants. The most efficient treatment he found to be the substitution of shorter intervals of feeding, three hours instead of four hours. This was continued only two to three weeks, when a return could be made to the longer intervals.

Rosenstern[10] and Langstein[8] are both averse to any general change in breast-feeding to shorter intervals, although in especial cases, as here, it is indicated; in their opinion the long intervals of feeding have done much to make possible the present increase in prevalence of breast-feeding. Other therapeutic measures advised by Rosenstern in this condition are: a temporary *"allaitement mixte"* which may often be discontinued after ten to twenty days; the giving after each feeding of breast-milk which has been pumped off; the administration of small amounts of pepsin and hydrochloric acid.

Langstein[8] advises buttermilk for *"allaitement mixte"* if the latter is necessary; and believes that it is unimportant whether the supplementary feeding be given after each nursing, or as separate feedings.

As a method for determining the amount of breast-milk taken by the infant the regular weighing before and after each feeding for two successive days is coming into general use; it is especially recommended by Langstein,[8] Rosenstern,[10] Jones[11] and others. Reuben[6] considers this method less practical than the weighing of the infant before and after a week on exclusive breast-feeding and noting the gain or loss.

Engel[15] has made an interesting observation relative to the souring of breast-milk. He finds that this depends to a large extent on the fat, and that the cream shows a much higher acidity than the whole milk.

On the subject of the wet-nurse problem, there have been interesting and practical studies by Hoobler, Talbot and Lee. Hoobler[12] reports the results of a successful experiment in the collection of human milk for hospitals, from women who came to the hospital once or twice daily. He believes that it is possible to obtain breast-milk in this way at a moderate price in any hospital, through cooperation with the Social Service Department.

Lee[14] tells of the excellent results which were obtained in a series of foundlings under the care of wet-nurses. Of thirty-one infants, twenty-three developed well; of these many had been extremely atrophic infants.

Talbot[13] describes the very successful wet-nurse directory established under the supervision of the Massachusetts Babies' Hospital.

ARTIFICIAL FEEDING

General

17. Howland: Am. Jour. Dis. Child., 1913, v, 390.
18. Rosenstern: Ergebn. d. inn. Med. u. Kinderh., 1911, vii, 337.
19. Morse: New York Med. Jour., 1913, xcvii, 477.
20. Lederer: Ztschr. f. Kinderh., 1914, x, 90.
21. Schloss: Ueber Saulings ernährung, Berlin, 1912, Karger.
22. Leopold: Arch. Pediat., 1914, xxxi, 20.
23. Barhdt: Jahrb. f. Kinderh., 1913, lxxviii, 598.

24. Barhdt and Edelstein: Ztschr. f. Kinderh., 1914, x, 303.
25. Langstein: Jahreskurs f. Aerztl. Fortbild., 1913, iv, No. 6.
26. Rulison: Arch. Pediat., 1913, xxx, 762.
27. Phillipson: Monatschr. f. Kinderh., 1913, xii.
28. Reinach: Ztschr. f. Kinderh., Ref., 1914, vii, 397.

Howland[17] considers our guides in infant feeding in regard to the amounts to be given. He criticizes the caloric standard, as the energy quotient of 100 calories pro kg. body-weight was first determined on the basis of calorimetric observations made on children at rest. He has shown that the heat elimination of infants crying or making active movements is 18 to 39 per cent. greater than that of those at rest; so that by this method one cannot learn the total amount of energy that should be furnished the normal growing child. He criticizes also the statistical method, in which the intake of food of normal thriving breast-fed infants has been systematically measured for long periods, on the ground that the composition and hence the caloric value of breast-milk varies greatly.

Rosenstern[18] has made clinical observations on many artificially fed infants, and has found that 100 calories pro kg. of body-weight is sufficient for a normal gain on diets which are poor in fat and rich in sugar; while on those with much fat and low sugar more calories are needed. He advises an increased energy quotient for premature and atrophic infants. Langstein[8] comes to the same conclusion. The same authors discuss the importance of the various constituents of cow's milk, in the artificial feeding of the infant. The water content is of the first importance, the salts and carbohydrate next, gain in weight and water retention being to a large degree dependent on the salt and sugar content. Rosenstern believes that knowledge of this fact is of great practical importance at the present time, when so many of the therapeutic foods are based on the principle of a reduction of the whey content. The loss in weight of a child changed to a diet poor in salt is the greater the richer the previous diet was in this constituent. A child changed from a diet rich in salt to breast-milk, which is comparatively poor in salt, will show a loss in weight. Carbohydrates are absolutely essential to life. The minimum amount of sugar that it is safe to give varies with different children, but is placed by these authors at 1.5 per cent. Without carbohydrates a gain in weight is impossible. Proteid is apparently necessary in smaller percentage than is sugar, as shown by its relatively low content in breast-milk. Fat they believe to be entirely replacable by carbohydrates; children have been fed on fat-free mixtures for months without symptoms, in case the caloric needs are covered.

Czerny agrees that gain in weight depends on the carbohydrates, but does not agree that it is proven that fat may be entirely replaced

by carbohydrate without harm; Morse[19] and others believe that fat is of great importance, especially to the young infant.

Lederer[20] has studied the importance of water to the infant metabolism.

The relation between artificial feeding and a decrease in the immunity to infections has been the subject of considerable study. Czerny[2] has studied the relation of natural immunity to different foodstuffs. He quotes the animal experiments of Weigert, which showed that those fed on high percentages of fat have the greatest resistance against tuberculosis, while those on high carbohydrates have the least. Czerny has found that children fed on diets rich in fats (including breast-milk) have the greatest resistance to infection, while children on diets rich in carbohydrates, but poor in fat, have the least natural resistance. The latter fact he attributes to the greater water content of the tissues on this diet; a high water content being always associated with low natural immunity. Kleinschmidt[1] studied this subject by observing in animals the effects of different foods on the formation of certain antibodies, such as hemolysins, agglutinins and bacteriocidins. He found that young dogs on diets rich in carbohydrates or fat did not necessarily show any diminution in antibody formation, but that the dogs who acquired disturbances of nutrition on these artificial diets did show a decrease in hemolysins, which returned to normal during convalescence.

Artificial Feeding of the Normal Infant

Morse[19] advises feeding by the percentage method, as thereby greater individualization of cases may be practiced.

The simple dilutions of milk (one-third, one-half, two-thirds) with water or barley water, enriched with carbohydrate, are recommended by various writers: Rulison,[26] Philippson,[27] Reuben.[6] They are in general use in Germany, and are becoming widely used in this country. On account of their simplicity they are generally used in feeding at Infant Welfare stations. The relative value of the various sugars is treated below in another connection. The early addition of fruit juices and vegetable purées to the diet (at the seventh or eighth month) has been recommended again by Langstein.[25] In the feeding of children from 1 to 3 years of age he urges the reduction of the amount of milk taken, the addition of larger amounts of fruit and vegetables, with meat in the second year, and the avoidance of eggs.

Efforts are being continually made to prepare a diet for normal children superior to the simple milk dilutions; the most important of this class are the Friedenthal milk and the "whey-adapted" milk of Schloss. Both were originated with the purpose of imitating breast-milk as nearly as possible. In both a marked dilution of the salt con-

tent is a principal feature. Friedenthal, according to Bahrdt,[23, 24] has ignored recent findings as to the dangers of fermentation of lactose, and those of a high fat content, and has simply attempted an imitation of the composition of breast-milk. Schloss, he says, at first used this milk, but not finding it successful, developed from it his own whey-adapted milk, which is in reality entirely different. Friedenthal's milk consists of the following ingredients:

Skimmed milk	330	c.c.
Water	660	c.c.
Lactose	68.9	gm.
"Molkerei" salts	1.89	gm.
Fat (in cream) to	4.5	per cent.

The "molkerei salts" consist of two parts KCl, one part K_2HPO_4 and one part KH_2PO_4. These are added to bring the composition of the mixture in regard to the separate salts as near as possible to that of breast-milk. At first only the cream was pasteurized, the milk being sterilized by centrifuging; but as the bacterial count was found to be very high the milk also was pasteurized during July and August. Bad effects from the milk, even when showing an extremely high count, were not frequent. Bahrdt believes that this has a bearing on the question of the relation of bacterial contamination of milk to summer diarrhea. In its composition as compared with that of breast-milk it shows equal percentages of fat and lactose, while those of proteid and salt are higher. This diet was given to 150 children; of these eighty-nine were considered in the review. Among these were healthy, newborn, premature and sick infants. The results as to gain in weight, confirmed by the good retention of nitrogen and ash in prolonged metabolism experiments, were very satisfactory. In the healthy children the average weekly gain was 123 gm. No immunity to parenteral infections is conferred by this food, but it is noticed that the infants pass through them with little disturbance of nutrition. Frequently there is vomiting, and the stools are often abnormal, apparently without clinical significance, resembling in this respect the stools of breast-fed infants. Bahrdt and Edelstein conclude that Friedenthal's theory of the benefits of a food approximating breast-milk in composition has been proved true in practice, and that the food has been shown to be far superior to simple milk dilutions as a food for normal infants.

Langstein[25] warmly recommends the Friedenthal milk. Confirmation from other sources has not so far appeared; in a matter of this importance it is to be anxiously awaited.

The "whey-modified milk" of Schloss[21] is essentially a diet rich in fat and proteid, poor in salt, with the addition of carbohydrates which

are not easily fermented. It resembles the group of substitutes for albumin milk to be later described; but differs in that it was developed in an attempt to imitate breast-milk. To milk diluted with twice the amount of water is added fat, in the form of cream, proteid in that of the preparations "nutrose" or "plasmon;" the carbohydrates added are a very finely ground maize flour and *Nährzucker* (dextrin-maltose). In addition a small amount of potassium chlorid is added. Schloss fed two hundred infants on this food for about a year with very good results; the development, color and stools all being normal.

Leopold[22] describes the preparation of this food as recommended by Schloss and reports a series of thirty cases, which were, however, not normal; all had nutritional disturbances. In no case did he see harm from its use. It appeared especially indicated in young infants, while older children often showed no gain.

Reinach[28] has also used this food; his results in normal infants were but moderately successful when the food was used alone; when it was used as *"allaitement-mixte"* they were more successful. He, too, saw the weight stationary for long periods; it increased, however, when sugar was added. Of twenty-one cases of sick infants on this feeding, sixteen showed recovery.

ARTIFICIAL FEEDING OF THE SICK INFANT

29. Benfey: Jahrb. f. Kinderh., 1913, lxxvii, 475.
30. Finkelstein and Meyer: Monatschr. f. Kinderh., 1909, viii, 8.
31. Finkelstein and Meyer: Jahrb. f. Kinderh., 1910, lxxi, 525.
32. Finkelstein and Meyer: München. med. Wchnschr., 1911, lviii, 315.
33. Meyer: Jahrb. f. Kinderh., 1913, lxxvii, 85.
34. Wilcox and Hill: Am. Jour. Dis. Child., 1913, v, 297.
35. Hoobler: Am. Jour. Dis. Child., 1913, v, 308.
36. Meyer: Halbmonatschr. f. soziale Hygiene u. Prakt. Med., 1912, No. 9.
37. Nobécourt and Schreiber: Bull. de la Soc. de Pédiat., 1913, xv, No. 7.
38. Ribadeau: Nourrison, 1913, i, 162.
39. Beck: Klin.-therap. Wchnschr., 1913, xxv, 740.
40. Heim and John: Ztschr. f. Kinderh., 1912, iv, 1; Heim and John: Monatschr. f. Kinderh., 1913, xi.
41. Frank: Monatschr. f. Kinderh., 1913, xii, 151.
42. Engel: Deutsch. med. Wchnschr., 1913, xxxix, 1251.
43. Engel: Jahrb. f. Kinderh., 1913, lxxviii, 299.
49. Hoobler: Arch. Pediat., 1914, xxxi, 174.
50. Aschenheim: Monatschr. f. Kinderh., 1913, xii, 229.
51. Steinitz and Weigert: Monatschr. f. Kinderh., 1913, xii, 243.

The interest this year has centered about the group of albumin milk and its substitutes. Whey and whey-soup have also been used. There are few new publications on buttermilk or on malt-soup.

ALBUMIN MILK

Albumin milk has now been proved to be of the greatest value as a therapeutic food in the nutritional disturbances of infancy. This is shown not only by its widespread use, but also by the large numbers of substitutes and imitations, descriptions of which have dominated the literature on infant feeding for this year.

Benfey[29] gives a careful review of the literature on albumin milk from its introduction in 1909 until April, 1913. Finkelstein and Meyer, he says, in their first publication, described its essential qualities as consisting of a high percentage of proteid, with a moderately high fat content, and a very low percentage of the salts and of milk-sugar. The chief benefits of the food are a reduction of fermentation in the intestine, and a substitution for it of putrefactive changes, leading to the characteristic calcium soap stools. With the cessation of diarrhea a gain in weight is made possible; also an increase in tolerance to all foods occurs.

Finkelstein and Meyer[30, 31] in their earliest publications, advised its administration at first without carbohydrate; this was to be added later only when the stools became normal. After much clinical observation they have, however, become convinced of the great dangers of too complete and too prolonged withdrawal of carbohydrates, as leading to marked initial losses in weight, with later stationary or gradually falling weight. In their later publications,[32, 36] therefore, they advise that albumin milk without sugar should not be used; 1 per cent. of sugar should be given at first and this should be rapidly increased to 2 to 3 per cent., and later, if there is no gain in weight, to higher amounts. Benfey adds from his experience at Finkelstein's clinic that there albumin milk with less than 3 per cent. sugar is never used. As explaining this procedure, the authors maintain that in the medium of albumin milk, sugar is tolerated in amounts that cause trouble when given in other media; as sugar is essential for a gain in weight, this is one of the chief advantages of the food.

Benfey reviews, at some length, the results of different observers with albumin milk from the time of its introduction. As the first series of cases were all treated according to the first directions of the originators, that is, with a very late and meager addition of carbohydrates, Benfey believes that they do not give a fair picture of what can be accomplished with this food. The results were, on the whole, favorable, and many authors expressed the opinion that albumin milk is a valuable aid in all nutritional disturbances. The reports from other countries, as from France and America, have been less favorable than those from Germany; there, however, he believes, the fear of giving carbohydrates has persisted longer. In the series from these

sources, in which exact data as to dosage are given, Benfey has found errors in technic, especially in the giving of too little carbohydrate, or in beginning too late, or in withdrawing it a second time. In reports in which no data are given, he assumes that the same errors in technic are at fault. He quotes Finkelstein as saying that no one should express an adverse opinion on albumin milk, who has not followed the later instructions as to dosage. Benfey concludes that the general opinion of the majority of authors is that they can obtain results in certain cases with albumin milk which cannot be achieved with any other form of artificial nourishment. The chief criticisms of the food are:

1. Its costliness, if obtained at a laboratory, and its difficult preparation if it is made in the hospital or home.

2. Its disagreeable taste and appearance.

3. An alleged tendency to cause eczema, and also one to cause rachitis or Barlow's disease, if fed for too long periods.

4. Poor results obtained in disturbances resembling dysentery.

He adds a valuable résumé of the indications for use, and the technic of feeding of albumin milk according to the present status of experience.

Indications for Albumin Milk

Albumin milk he believes to be indicated in all disturbances of infants accompaned by diarrhea, including these disturbances when associated with parenteral infections; also in all nutritional disturbances not reacting to other forms of artificial feeding. This includes true bacterial enteritis, in which Finkelstein has achieved very good results in spite of some adverse criticisms by other writers. Only in "weight disturbance" (*Milchnährschaden* of Czerny) better results are obtained with mixtures rich in carbohydrates, such as malt-soup.

Technic for Use of Albumin Milk

1. In dyspepsia and decomposition: Weak tea only should be given for six hours; then albumin milk at the rate of 300 gm. in twenty-four hours with 3 per cent. *Nährzucker*. In mild cases and in older children even more should be given. The daily amount is then to be rapidly increased without respect to the stools or other symptoms until 180 to 200 gm. per kilogram of body-weight is given in twenty-four hours. After cessation of the diarrhea, the sugar is to be increased to 5 per cent.; when there is no further gain in weight, to 6, 7, or 8 per cent. In children over 3 months flour should be added in the amount of 1 per cent.

In subtoxic cases, or those on the borderline between dyspepsia and intoxication, the amount should be only 150 to 200 gm. for the first

twenty-four hours with 3 per cent. sugar; the increase should then be more gradual, as in intoxication.

2. Intoxication: Weak tea only is given for twelve to twenty-four hours; then for twenty-four hours ten feedings of 5 gm. of albumin milk with 3 per cent. sugar, after each of which large amounts of water or tea should be given. The amount should then be increased very gradually by 50 gm. daily, until severe diarrhea stops; after which a more rapid increase should daily be made until the amount of 180 to 200 gm. per kilogram body-weight is reached. At this point at latest, the carbohydrates should be increased; but if meanwhile the fall in weight has not stopped, carbohydrates should be added earlier. In case diminution of the toxic symptoms does not occur, the amount should be increased only to the point of 130 to 150 gm. per kilogram body-weight with 3 per cent. sugar; at this point one should stop until toxic symptoms disappear. An attempt to bring about lessening of the toxic symptoms by a second withdrawal of food is extremely dangerous and often fatal. Benfey warns against the use of albumin milk combined with any other food. It has been much used as *"allaitement mixte"* with human milk; but here he believes the results with buttermilk are better.

The cause of the beneficial results of albumin milk has been considerably discussed, especially in relation to the substitutes. The general result is a change in the predominating bacterial flora of the intestine; bacteria of the fermentative group lose the ascendency, which is gained by those of the putrefactive group; this condition is far more favorable and permits the formation of soap stools with foul odor. The elements favoring this change are, according to the early publications, the high percentage of proteid, and the low percentage of salt and of milk-sugar.

Stoeltzner[44] believes that the success of certain substitutes proves that the diminution in salt and sugar, also the large amount of fat, are of minor importance; that the feature of albumin milk essential to its success is the high content of proteid and calcium.

Wilcox and Hill[34] report on results with a modification of albumin milk, in whose preparation skimmed milk was used, the fat content consequently being very low. In its administration they did not follow the rules laid down by Finkelstein, as they omitted the preliminary time of hunger or tea diet; did not add sugar at once, but only after an improvement in the stools. They used the albumin milk only as a corrective and only for short periods, as they found that gain in weight followed very slowly or not at all.

Hoobler[35] studied the metabolism of children fed on protein milk made in this way, having the following composition: proteid 2.8 per

cent., carbohydrates 2.4 per cent., fat .8 per cent. He found that on this large amount of proteid the nitrogen intake was increased over the normal, and its retention good, being 27 to 35 per cent. He quotes the important findings of Holt and Levene as to the clinical composition of the stools on diets high in protein, showing a decrease in acidity, together with one in the volatile fatty acids, a great increase in the soaps, with an improved retention of the mineral salts and a decrease in the amount of water lost.

G. Meyer[33] reports on the successful use of albumin milk in dispensary work; he favors a slight modification of technic, as follows: Children who are markedly atrophic should be given more than the usual 200 gm. per kilogram body-weight; sugar should not be added in larger amounts than 5 per cent.

Two more unfavorable reports on albumin milk have come recently from France. Nobécourt and Schreiber[37] think it illogical to suppress the lactose of the milk and add maltose. They believe the absence of sugar is dangerous. They administered the food in twenty-one cases, with good results in only two.

Ribadeau[38] saw bad effects, characterized by a sudden collapse with coma, after the use of albumin milk, even though he had followed exactly directions as to its use.

Beck[39] reports a series of 300 cases of nutritional disturbance treated with this food. He believes that there is at present no other artificial food which, in severe sickness, leads to recovery with such rapidity, certainty and frequency as does albumin milk.

SUBSTITUTES FOR ALBUMIN MILK

The faults of albumin milk previously referred to, particularly its expensive and difficult preparation, have limited its usefulness, especially in private practice. Here it is almost excluded except in cities with milk laboratories and among the rich. Its other disadvantages, such as its unattractive appearance and taste and its tendency to clump unless very carefully heated, are of less importance, but are definite drawbacks. Hence many pediatricians have been striving to originate foods without these disadvantages, yet incorporating its essential principles, and giving the same results. Many of these substitutes have been introduced, and for many of them results "at least as good" as those of albumin milk have been claimed; yet I believe until the results are more fully corroborated, those who can obtain albumin milk will continue to use it. To those who are not able to obtain it, one or the other of these simpler substitutes are recommended.

The first modification was that of Heim and John,[40] who on account of difficulty in obtaining good buttermilk used in its stead

skimmed milk diluted one-half or two-thirds with water, to one liter of which the curd, that is the proteid, fat and calcium, from two-thirds of a liter of whole milk was added after fine subdivision through a sieve. The essential feature is then the substitution of skimmed milk for buttermilk. They give the histories of cases receiving this feeding, with results resembling those of albumin milk.

Frank[41] made comparative metabolism experiments comparing children fed on diluted whole milk with three children fed on milk enriched with casein and fat as above. The conclusions are that on this feeding carbohydrate absorption is good, the retention of nitrogen normal, the fat resorption normal.

Engel[42, 43] finds that Heim and John's preparation is still too difficult for practical use, as it involves the fine subdivision of the curd through a sieve. This he attempts to avoid by very careful dosage of the lab ferment; by this means he obtains a curd with fine flocculi. He then dilutes the mixture with an equal amount of water, and after the casein flocculi have settled, pours off one-half of the supernatant fluid. He obtains a mixture in which the whey is diluted one-half, while there is a relatively high percentage of proteid, fat and calcium. He advises the use of this casein milk in the same amounts as those advised for albumin milk, with the same additions of sugar.

On comparison of the composition of this diet with that of albumin milk, it is shown that the percentages of proteid and fat are the same, but that those of sugar and calcium are higher in the casein milk. His results, in nine months' use, are, he says, as good as those with albumin milk.

Hoobler[49] has used a modification in which he employs casein flour. This he adds in the amount of 10 gm. to one pint of fat-free buttermilk and one quart of warm water. In some cases he uses the artificial buttermilk, which contains fat. With this preparation he has attained very good results. Its chief advantages are its cheapness, and ease of preparation, recommending it for private and dispensary practice.

Aschenheim,[50] led by the importance of calcium in the formation of the firm soap stools, tried adding calcium in the amount of 7 to 10 gm. in 10 per cent. solution to the diet. He gave it in all types of nutritional disturbances, and never saw any unfavorable symptoms; the results were fairly good, but not to be compared with those of albumin milk. The best results were obtained in dyspepsia, the worst in dyspepsia caused by parenteral infections.

Steinitz and Weigert,[51] seeking a diet very poor in fat for use in acute disturbances have used "whey-soup," which is merely whey to which 4 per cent. mondamin is added. They use it with good results in the same way that Stolte used buttermilk with mondamin, giving only one to three feedings daily of this preparation, the other feedings being simple milk dilutions.

STARVATION

Some extremely interesting work is that done chiefly by Finkelstein, Meyer, Rosenstern and Langstein on the subject of the importance of starvation to the infant. A good deal of this work dates back to 1911 and 1912, but has not been reviewed in this journal.

In an excellent review of all the work done on this subject, together with an account of his own clinical observations, Rosenstern[18] says that at the present time the good effects of starvation are so generally accepted that its dangers are neglected. The latter are not important to the healthy infant, but are extremely great to the sick child. In atrophic babies, hunger often leads to a fatal collapse; so that in these cases a tea or water diet should not be given at all, but small amounts of food from the beginning. Also in overfed children, especially those previously on a high percentage of carbohydrates, starvation will sometimes lead to an extreme and even dangerous loss in weight. Starvation as a therapeutic measure is most successful in acute disturbances, such as dyspepsia and intoxication; it is dangerous in chronic and recurrent affections. When used as a therapeutic measure, the following procedure should be employed: complete hunger for a short space of time, followed by small amounts of food, which are rapidly increased. The opposite procedure, with a gradual diminution in the amount of food given, leads, as he demonstrates by charts, to much greater losses in weight. He warns against this method, as well as against the starving of an infant many times in succession. Langstein[8] has confirmed and amplified this work.

The qualitative starvation in different foodstuffs is considered by both; water, sugar and salt starvation are the most important and dangerous.

THE NUTRITIONAL DISTURBANCES OF INFANTS

52. Dunn: Boston Med. and Surg. Jour., 1913, clxviii, 161, 168.
53. Finkelstein: Ztschr. f. Kinderh., 1913, vii, 67.
54. Smith: Boston Med. and Surg. Jour., 1913, clxix, 756.
55. Koplik: Arch. Pediat., 1913, xxx, 484.

The majority of American authors believe that our present classifications of the nutritional disturbances are temporary and will soon be changed.[55, 19] Dunn[52] classifies them, on an etiological basis, into two chief types:

1. Those caused by foodstuffs: fat, carbohydrates, proteid, salt. Within this main group he includes two sub-groups:

a Those caused by abnormal digestion or absorption of several foodstuffs, especially fat and proteid, shown by vomiting and dyspeptic stools, the treatment for which consists in a reduction of these substances.

b A little understood group, characterized by intolerance to salt, fat and milk-sugar; which is best treated with a diet containing little fat and sugar, and much casein.

2. Disturbances caused by bacterial infections. Of these the majority of the causative agents, except dysentery and gas bacilli, are unknown. They are best treated with buttermilk.

Smith[54] gives a similar classification. Finkelstein[53] has expanded and modified his former classification, without, however, changing its main features. He considers the introduction of the term "nutritional disturbances" as of value; but thinks that at present too many heterogeneous conditions are included under the term. He divides the "alimentary disorders" into two main classes:

1. Nutritional disturbances due to an error in diet; that is, to an exogenous cause.

2. Nutritional disturbances from endogenous causes, such as essential anomalies of growth and development, and to constitutional diseases, such as rachitis and spasmophilia.

Finkelstein does not believe that these disturbances can best be classified on an etiological basis, as has been done by Czerny; for he shows that in the causation of any disturbance many factors combine as nutrition, infection, constitution, heat, etc., and that rarely has a disturbance but one cause. Hence he uses as a basis for his classification the essential clinical features, using the etiology, however, as a secondary means of differentiation. The group of nutritional disturbances of exogenous cause he divides into (1) dystrophies, or conditions due to faults in diet, without marked disturbances of the gastro-intestinal function. This includes several types of the "*Bilanzstörung*" of his older classification. (2) Alimentary toxicoses, which do show gastro-intestinal and metabolic disturbances, such as diarrhea and marked losses in weight. These include the less and more serious conditions: dyspepsia, decomposition and intoxication. All these may arise from a purely alimentary basis; or from a mixed cause, alimentary and infectious. In disturbances from the latter cause the prognosis is far more serious, as the ability of the organism to secrete digestive juices and ferments is decreased and internal metabolism is attacked. He believes that the colloids in close relation to carbohydrate and salt metabolism are so changed that the salt and water content of the organism is threatened.

Etiology

56. Howland: Am. Jour. Dis. Child., 1913, v, 390.
57. Langstein: Jahreskurs. f. Aertzl., Fortbldg., 1913, vii, No. 6.
58. Feer: Jahrb. f. Kinderh., 1913, lxxvii, 1.
59. Jörgensen: Monatschr. f. Kinderh., 1913, xii, 386.
60. Wood: Arch. Pediat., 1914, xxxi, 259.

61. Bendix: Ztschr. f. Kinderh., 1913, vi, 468.
62. Klotz: Ergebn. d. inn. Med. v. Kinderh., 1912, viii, 593.
63. Morse: Jour. Am. Med. Assn., 1913, x, 875.
64. Talbot: Arch. Pediat., 1913, xxx, 244.
65. Southworth: Arch. Pediat., 1913, xxx, 732.
66. Holt and Levene: Med. Klin., 1913, ix, 258.
67. Neuhaus and Schaub: Ztschr. f. Kinderh., 1913, vii, 310.
68. Lust: Jahrb. f. Kinderh., 1913, lxxvii, 383.
69. Calvary: Ergebn. d. inn. Med. u. Kinderh., 1913, x, 699.
70. Hahn: Jahrb. f. Kinderh., 1913, lxxvii, 405.
71. Hess: Am. Jour. Dis. Child., 1913, v, 457.
72. Grulee: Jour. Am. Med. Assn., 1913, lxi, 1022.
73. Gildemeister and Baerthlein: Deutsch. med. Wchnschr., 1913, xxxix, 982.
74. Vaughan: Jour. Am. Med. Assn., 1913, lxi, 1761.
75. Baerthlein and Huwald: Deutsch. med. Wchnschr., 1914, xl, 478.
76. Bauer, Ellenbeck and Fromme: Arch. f. Kinderh., 1913, lxi, 35.
77. Siegel: Arch. f. Kinderh., 1913, lx-lxi, 689.
78. Weihe and Shürer: Ztschr. f. Kinderh., 1914, x, 36.
79. Smith: Boston Med. and Surg. Jour., 1913, clxix, 756.
80. Kendall: Boston Med. and Surg. Jour., 1913, clxix, 741, 749, 754.
81. Vincent: Arch. Pediat., 1914, xxxi, 53.
82. Vincent: Am. Jour. Dis. Child., 1914, vii, 97.
83. Vincent: Am. Jour. Obst., 1913, lxviii, 1204.
84. Keuper: München. med. Wchnschr., 1914, lxi, 474.
85. Bowditch: Arch. Pediat., 1913, xxx, 866.

The views of the different schools of pediatrics as to the etiology of the nutritional disturbances of infants are becoming gradually reconciled, as there has come to be a general agreement that the principal cause may be either one of two general causes: food or bacterial infection. In Germany the chief prominence is given to the influence of the different food elements, together with the predisposing action of certain other factors, such as hot weather and parenteral infections; yet there, too, there has been a great increase in interest in the intestinal infections, especially of the dysentery group. In America, on the other hand, while the influence of the different bacterial infections is still considered of the greatest importance, especially in the etiology of the summer diarrheas, yet there is greater interest than before in the harmful action of the foodstuffs.

Influence of Food and Foodstuffs

Howland[56] gives a valuable critical review of our present knowledge of the rôle of the different elements—proteid, fat, carbohydrate and salt—in the causation of these disturbances, and shows how on each in turn has fallen the blame. The damaging influence of sugar and salt, now given the principal place as causing the acute disturbances, may, he considers, be exaggerated.

Langstein[57] and Feer[58] both believe that separate food elements should no longer be considered the primary causes of the nutritional disturbances, but rather a faulty correlation between them. Lang-

stein believes the ingredient of chief importance in cow's milk is the whey (or salts and sugar in solution). He quotes Meyer's well known "whey exchange" experiment in proof of this. The combination of a high whey content with a high sugar and low proteid percentage causes the greatest number of nutritional disturbances. Increase of the proteid reduces the danger. A high percentage of whey can be tolerated if the sugar is low; of such diets buttermilk is an example. The cause of this is unknown, according to Langstein; two possibilities may be considered: that the whey is injurious to the intestinal wall, and causes a greater permeability for various substances; or that the whey stimulates carbohydrate fermentation.

Feer, on the other hand, thinks the relation between fat and whey is most important; mixtures rich in both fat and whey are harmful, but after removal of the fat they are well borne.

Salts

The rôle of the salts, in combination, as above, with sugar or fat, is at present in Germany placed in the highest position of importance as the damaging substance in cow's milk. Its reduction is the foundation both of the proposed normal foods for infants, such as the Friedenthal milk and Schloss's whey adapted milk, and of the chief therapeutic foods, such as albumin milk and its substitutes. The chief theory of its harmful action is the second named by Langstein: that it favors acid fermentation by bacteria of carbohydrate if this is present in large amount, with the production of an excess of the low fatty acids and the consequent irritation of the intestine. Large amounts of proteid change the process to one of putrefaction.

Salt fever, or the temperature previously caused by parenteral injections of salt solution, has again been proved by Jörgensen[59] not to occur, if the water used as diluent for the salt solution be freshly distilled and sterile. This had previously been shown by several observers, among them Samelson and Bendix. Hence a direct fever produced by salt seems excluded. Wood[60] has reviewed the rôles of the salts in the infant's nutrition.

Carbohydrates

The action of the carbohydrates as related to that of the salts has already been reviewed. Some difference of opinion still exists as to the comparative harmfulness of the different sugars. Lactose is recommended by Morse[19] as the least harmful. The various combinations of maltose with dextrin are most often advised by German authors. Calvary considers lactose as good as cane-sugar. Bendix[61] fed different forms of sugar to thirteen infants in order to determine which caused the least trouble. He found, contrary to the usual findings,

that cane-sugar caused the least fermentation, lactose the most, while maltose held a position midway between the two. Maltose, however, led to a greater gain in weight. He strongly advises the use of cane-sugar on account of its cheapness. Klotz[62] has found that the various flours vary greatly in their properties but so far the indications for the various flours are not certain.

As to the much discussed "sugar fever," Kleinschmidt[69] showed that on intravenous injection in rabbits of an isotonic dextrose solution, the diluent of which was freshly distilled water, he obtained no rise of temperature. With an isotonic lactose solution he did, however, obtain a rise of temperature which he believes may be due to bacteria in the milk-sugar.

Fat

The rôle of fats as an exciting cause of the nutritional disturbances is given varying importance by different writers. The point is still unsettled whether acute dyspepsia is or is not caused by fat. Feer, as before shown, believes that fat in a medium containing a high whey percentage may cause acute disturbance. Dunn[52] believes that there are acute disturbances due to fat, shown by vomiting and dyspeptic stools. Talbot[64] writes that there is an indigestion due to fat, the symptoms of which may be identical with those of one caused by sugar or protein, so that information as to the cause must be drawn from the vomitus and the stools. The vomitus he describes in these cases as creamy, while the stools macroscopically show soft curds, and microscopically much fat and soap. He adds the description of a staining method by means of which the proportionate amounts of fat, fatty acids and soaps can be determined. The action of fat as tending to induce vomiting and delay of food in the stomach has long been considered well established. The comparison of the gastric mobility with different foods by Ladd[127] tends rather to show that fat has less effect in the latter direction than casein.

The chief disturbance caused by fat is still considered that chronic condition known as *"Milchnährschaden," "Bilanzstörung,"* or "weight disturbance." This is reiterated by Finkelstein, Howland, Langstein, Feer and others.

Southworth[65] calls attention to a closely related symptom, the ammoniacal odor of the diaper in certain infants receiving a large amount of fat. The explanation, he believes, is to be found in the metabolic changes described by Czerny in that condition. The essential change is an increase in acid formation, and the using up to neutralize it of fixed alkalies and of ammonia. The ammonia salts are excreted in the urine, to which they give the characteristic odor. As

the acid may also be neutralized by alkali taken by mouth, he finds that the trouble readily yields on the administration of alkalies while the percentage of fat is reduced. He reports five cases, fed on high percentages of fat, showing an ammoniacal odor of the urine which disappeared on this treatment.

Proteid

Morse[19] does not believe that proteid is entirely harmless, while most of the German writers, among them Langstein, do consider it so. Combé has described a dyspepsia caused by albumin. Holt and Levene[66] have found that large amounts of casein by mouth can cause a rise in temperature. During the course of experiments in which a "synthetic food" very rich in casein was fed, they observed five times a rise in temperature, which continued until the food was changed, but then subsided to normal. This fever only occurred when 6 per cent. casein had been administered, with very small amounts of milk. Preceding the rise by three or four days and accompanying it, there was in all cases a retention of the chlorids. Other causes for this fever, such as salts, or a possible change in the intestinal flora, the authors believe are excluded. They call attention to the parallelism between this fever and that produced by Vaughan by the parenteral injection of proteins.

The association of anaphylaxis with some of the disturbances caused by cow's milk has always been a field for speculation; but so far the evidence has been very meager and inconclusive. Neuhaus and Schaub[67] report an interesting case, suggestive in this connection. A healthy child who had previously been breast-fed, but who had probably received small amounts of cow's milk, became very ill when he received a large amount of cow's milk. The symptoms were suggestive of anaphylactic shock, and there were large numbers of eosinophils in the stools. After recovery, a similar attack was induced by feeding casein from cow's milk, while casein from breast-milk and the whey from cow's milk had no effect. Later the child showed perfect tolerance to cow's-milk casein.

Hypersensitiveness to cow's milk could not exist without a passage of protein unchanged through the intestinal wall; this has been proved not to occur in the normal infant after the first weeks. That an increased permeability of the gastro-intestinal epithelium for foreign proteid occurs in children with nutritional disturbances has been proved by Hahn and Lust. Lust[68] fed different forms of foreign proteid to children with such disturbances, and then employed the following tests to determine whether or not the protein had passed through the intestinal wall unchanged: the urine, and in some cases the blood serum, were tested with a serum having a strong precipitation titer for

the protein which had been fed; also guinea-pigs were injected with the urine and after three weeks tested with the homologous protein for sensitization. He also studied the permeability in animals in which a gastro-enteritis had been produced by a strong sugar solution. In the experiments on infants he found that egg albumin passed through the wall nine times out of sixteen cases of acute and chronic nutritional disturbances, while ox serum passed once only out of seventeen cases, the passage being most frequent in acute intestinal disturbances, especially intoxication. The normal protective forces of the organism against the absorption of unchanged protein consist in two things: digestion of the proteid by gastric and pancreatic juices; and the normal resistance of the epithelial cells of the intestine to the passage of the protein. In nutritional disturbances, as the digestive juices are present, the fault must lie in the decreased resistance of these cells. He claims for his method considerable clinical value as a functional test of the condition of the intestine in nutritional disturbances. Hahn[70] has brought additional evidence to the same point, in his study of the passage of antitoxin bound to heterologous protein. It had been previously shown that the normal infant will absorb antitoxin given orally if bound to a homologous proteid, that is, if present in its mother's milk; but will not absorb it if bound to a heterologous protein, that is, horse serum. Hahn used Römer's test for the presence of antitoxin in the blood of infants to whom he fed horse serum antitoxin. Out of twenty-three cases all showing acute nutritional disturbances, there was in five a passage of antitoxin into the blood.

Vaughan[74] suggests an interesting possibility as to the cause of infantile diarrhea. He calls attention to the fact that peptone and other decomposition products of proteid cause symptoms of disease, and that "sensitization may result from the absorption of undigested or partially digested proteins from the alimentary tract. Whether or not the summer diarrheas of infancy ever originate in this way is a question to which a positive answer cannot be given. There are some good reasons for suspecting that the lowered vitality of the infant by excessive heat may lead to the absorption of undigested proteins, and in this way cholera infantum and kindred diseases may be induced."

It seems to me not quite clear from these guarded statements, whether the possibility suggested is that of an anaphylaxis to milk, due to the passage of its unchanged proteins into the blood, and the consequent development of hypersensitiveness; or that of an absorption of toxic split products of protein through the intestinal wall. The latter is the possibility spoken of by Grulee[72] in the discussion to the above paper, and in a further article on the etiology

of ileocolitis. He recalls the fact that it has now been proved that salt and sugar on parenteral injection do not cause fever, thus undermining Finkelstein's theory that it is the abnormal absorption of these substances unchanged that produces the metabolic changes present in the nutritional disturbances. Salt and sugar in large amounts by mouth do, however, cause fever; Grulee suggests the possibility that these substances if given by mouth cause a change in the intestinal mucosa which allows absorption of the toxic products of protein decomposition from the intestine always present there. These may be endotoxins from bacteria, or may be the product of bacterial decomposition of protein. He suggests the intestinal mucus as a source of protein poisons independent of the food. Zahorsky,[74] in the discussion of Vaughan's paper states his belief that one form of diarrhea at present believed to depend on fermentation of the sugars, may possibly be due to absorption of the toxins mentioned by Vaughan. These theories, connecting the nutritional diseases with the protein toxins and with anaphylaxis are fascinating, but lack clinical and experimental proof; so that at present they remain only in the realm of conjecture.

The casein curds occasionally present in the stools of infants on unboiled milk continue to be the object of study. Hess[71] has studied the site and causes of their formation. He concludes that there are several methods of inhibiting their formation: boiling of the milk (pasteurization does not prevent), the addition of sodium citrate, sodium bicarbonate or calcium citrate. The site of formation is apparently the stomach for he has found that the inside of these curds is never bile-stained; and in addition that a child who regularly passed curds when on unboiled milk no longer passed them when the same food was fed into the duodenum through a duodenal catheter. He found that some children, out of many on the same food, passed them much more frequently than others. He believes them to have little clinical importance, as their presence has no influence on the general development.

Influence of Bacteria

The bacteriological examination of the stools of infants with nutritional disturbances has long been an extremely confused field of research. Many different organisms have been described as occurring in connection with the same clinical symptoms; besides this, there has been lack of correspondence between clinical symptoms and bacteriological findings. From this confusion there has gradually emerged one fairly well defined clinical picture, called by different names: enteritis follicularis, ileo-colitis, dysentery-like diarrhea, etc., and characterized by fever, prostration, diarrhea with blood, mucus and pus in the stools, and a tendency to spread by contagion. In Germany much has been

written this year on this type of diarrhea, and the tendency is to confirm the earlier findings of American authors as to the frequent occurrence of dysentery and pseudo-dysentery organisms in these cases. In America, on the other hand, this clinical syndrome is associated with bacterial infection in general; and other organisms, especially the gas bacillus and the streptococcus, besides the dysentery and pseudo-dysentery bacilli, have been found closely associated with it. One point, not yet settled to my knowledge, is the relative importance and frequency of this type of disturbance in proportion to the entire number of cases of diarrhea which occur.

This form of diarrhea has long been recognized in Germany as an entity, but the tendency has been to consider it as only rarely a specific infection, and more usually merely the result of prolonged injury by food, leading to anatomical changes in the intestine. This theory still prevails in the minds of most of the writers on the subject, as shown by their failure to make direct mention of specific infection as a cause of the disease.

Gildemeister and Baerthlein[73] made a systematic examination of the stools of 120 normal infants, and of seventy infants showing diarrheal disturbances. They did not study the cocci nor anaerobic organisms. For the differentiation of dysentery bacilli they used the usual cultural tests. The feces for examination they obtained by inserting a small sterile glass tube with rounded edges into the rectum. Among the seventy sick infants they found dysentery bacilli of the Y-type nine times; paratyphus four times; bacillus enteritides Gärtner, once. In all the cases in which dysentery bacilli were found the stools were very loose and contained mucus and blood. They did not, however, find the bacilli in all the cases showing these symptoms. Of the 120 normal cases, only two showed dysentery bacilli; the brother of one of these had clinical dysentery. The authors believe that some external factor, such as a change in diet may be necessary to give the organism pathogenic qualities.

They also found proteus, pyocyaneus and coli mutabile bacilli, besides a strain not previously described, more frequently in sick than in normal infants, but decline to draw conclusions.

Baerthlein and Huwald[75] continued the same study last year, using the same technic. Among seventy-two children they found dysentery bacilli twenty-one times, paratyphus seven times, pyocyaneus twelve times. They also found dysentery bacilli in one normal case. Agglutination of the homologous strain was positive in eleven cases. Few of the strains were of the Flexner group, which they consider rare in Germany. Clinically these twenty-one cases showed fever, prostration, great loss in weight and numerous defecations with blood and mucus.

Siegel[77] analyzes the clinical symptoms in the eight cases previously reported by Gildemeister and Baerthlein. In all but one there was blood and mucus in the stools. At post mortem the findings were those of enteritis follicularis; in only one was there loss of tissue. He concludes that there is a close relation between Y-dysentery infection and follicular enteritis.

Bauer, Ellenbeck and Fromme[76] report an epidemic in an asylum, in which the agglutination reactions in especial were studied. Artificially fed children only were attacked; of 29 children on the bottle, 22 showed a positive agglutination reaction for the Y-dysentery organism; of these 11 only had clinical symptoms. In 9 of these 11, dysentery bacilli were found in the stools. The epidemic broke out with great suddenness, all the children but one in one of the wards being affected. The authors conclude that the agglutination reaction is specific; namely, that a positive reaction is only obtained in cases which have or which have had dysentery; a negative reaction under one year does not, however, exclude dysentery. Infants, they find, are very susceptible, and strict isolation should be used.

Weihe and Schürer[78] give an interesting review of the question of dysentery infection in infants in Germany. They find that the leading text-books make very little mention of it. Two epidemics have been reported by Jehle and Leiner, but for the most part the reports of American investigators have not been corroborated. This they explain in part by the fact that the American authors in their reports did not distinguish between true primary bacterial infection and nutritional disturbances as well as parenteral infections. They also believe that the great labor involved in the study of these cases has deterred many from it. The authors examined the stools of eighty-five children with intestinal disease, twenty-two of whom showed clinical symptoms suggestive of dysentery. In eighteen of these they found pseudo-dysentery bacilli, for the most part of the Y-group. They consider that blood in the stools should always be considered a suspicious symptom, and that all cases showing it should be isolated. Agglutination tests in their cases were negative or at very low dilutions. They believe that all forms of the nutritional disturbances, such as decomposition, intoxication, etc., can be caused by it. At necropsy the cases showed the typical findings of enteritis follicularis.

Keuper[84] reports an epidemic of twenty cases, also two sporadic cases. In the majority of these the organism of Kruse was found. He insists especially on a long isolation period; that negative bacteriological findings on two successive days are not sufficient to warrant discharge; and that this organism, like the typhoid bacillus, may persist for long periods in the intestinal canal after clinical recovery. He

concludes that, as infants do not form agglutinins with any regularity, the serum test is useless for diagnostic purposes.

American authors have found not only organisms of the dysentery and pseudo-dysentery groups in infectious diarrhea, but also the gas bacillus, and probably the streptococcus; and believe that still others, as yet unknown, are also at times to blame.

Smith[79] says that the symptoms in all the infectious diarrheas are the same; they are those already described above in the German publications on enteritis follicularis. These infections can only be classified by means of a bacteriological examination of the stools, which is especially necessary as the treatment depends on the causative agent. In the dysentery infections high carbohydrate percentages should be fed with low protein; while in gas bacillus infection the sugar should be greatly increased and high protein percentages should be given. He says that a number of cases not showing the gas bacillus in the stools, did well on this treatment.

Bowditch[85] reviews the work of the Boston Floating Hospital in the study of the bacteriology of the intestinal diseases of infants for the past three years. He shows that different bacteria have predominated in different years.

Kendall[80] reports more in detail the same study, and speaks also of this variation from year to year. He believes that less is known of the etiology of summer diarrhea than ever; that previously a disturbance showing blood and pus in the stools was thought always to be caused by the dysentery group, but that it is now known that similar symptoms may be caused by a variety of intestinal bacteria; also that in cases with these symptoms, pathogenic bacteria may be absent.

In 1910 dysentery infections predominated, constituting 75 per cent. of those in which an organism was isolated. The gas bacillus and streptococcus were less frequently found.

In 1911, on the other hand, the streptococcus was present in 78 out of 146 cases; dysentery bacilli in 18, the gas bacillus in 33.

In 1912 the gas bacillus predominated, 53 out of 135 cases showing this, while dysentery was only present in 5 and the streptococcus in 6. The conditions necessary for the development of gas bacilli are: an excess of carbohydrate, and a deficiency of organisms capable of forming lactic acid in sufficient volume to inhibit their growth. The treatment in these infections which is theoretically correct, and which has proved itself of value is:

1. Restriction of carbohydrates.

2. The introduction of lactic acid in buttermilk, or of lactic acid producing organisms.

3. An increase in protein.

He shows that the pathogenic bacteria especially of the dysentery group may be found in normal cases.

Vincent[81, 82, 83] studied the action of bacteria in the etiology of diarrhea from a new point of view: that of the bacteria growing in raw and in boiled milk. This work has not, so far, been confirmed.

So much for the rôle of bacteria as the direct causes of intestinal disease in infants.

Their secondary rôle, through action on foodstuffs, has long been believed by the German school to be extremely important, especially as regards the fermentation of carbohydrate by certain bacteria, apparently favored by the presence of a high percentage of salts. This view is held without change, and is expressed in most of the publications cited on albumin milk and its substitutes.

Influence of Parenteral Infections on Nutritional Disturbances

86. Meyer, F.: Hospitalismus, Berlin, 1913, S. Karger.
87. Meyer, F.: Ztschr. f. Kinderh., 1913, vii, 233.
88. Meyer, F.: Berl. klin. Wchnschr., 1913, l, 775.
89. Müller: Abstr. in Jahrb. f. Kinderh., 1913, lxxiv, 450.
90. Langstein: Ztschr. f. Kinderh., 1913, vii, 193.
91. Chapell and Brown: Am. Jour. Dis. Child., 1914, vii, 380.
92. Triboulet: Bull. Soc. de Pédiat., 1913, xv, 281.

This year great interest has been shown in the marked influence exercised by infections, especially of the respiratory and urinary tract, on the origin and course of the nutritional disturbances in infants.

Meyer[86, 87, 88] has written a great deal on the subject. "Grippe" is a clinical term which he uses to include infections of the respiratory tract of non-specific etiology, including pharyngitis, coryza, otitis and bronchitis. It is, he thinks, the infection most disturbing to the normal nutritional condition, causing loss of appetite and all types of disturbances: dyspepsia, intoxication and decomposition. Next in importance is pyelocystitis. The younger the infant, the more easily does the disturbance arise; also the diet has an influence, as such disturbances are more frequent on those diets tending in themselves to cause fermentation and diarrhea, such as those with a high sugar and salt percentage. Meyer[88] found that in dogs in whom severe nasopharyngeal infections were produced, the secretion of gastric juice was greatly reduced. He believes that other secretory activities are also diminished during infections, and that this may explain the close relation between them and disturbances of nutrition.

The importance of respiratory infections or "grippe" in infants' hospitals or asylums as preventing success in feeding cases has long been studied. Heubner pointed out their importance fifteen years ago, and showed that they were an important factor in the general condition called hospitalism. During the present year much work has been

done on the prevention of these infections. Meyer[86, 87] finds that in infant hospitals and asylums the mortality is greater from respiratory infections than from nutritional disturbances. He finds that no child remaining in a certain infant asylum over one month fails to develop some form of infection, while those remaining longer show, on an average, one such a month. As many children are necessarily admitted with respiratory infections the question of greatest importance is, how to prevent transmission of the infection from one child to another. This involves the question of the usual way in which such infections are carried, whether by contact or by air infection. Though the theory of contact infection is at present most generally accepted, Meyer believes that many things speak for an air transmission, especially of respiratory infections. He used Lesage's fundamental idea that infections are usually air-borne and that currents of air are instrumental in spreading them (Müller[89]), in the construction of an isolation ward. This showed a central aisle with a row on either side of compartments or boxes separated by partitions of glass, or gauze stretched on frames, 6 feet high. The ventilation in the ward was reduced to the minimum consistent with having the air fit for use. Beyond the usual washing of the hands after handling each infant, no measures against contact infection were used; no change of gowns was made except in the case of whooping-cough, measles and varicella cases. Further precautions were the avoidance of much movement and talking in the rooms, and the prevention of infection from physician or nurse if suffering with coryza or bronchitis, by means of their withdrawal from duty or by their wearing a gauze mask. The results were extremely successful; in two wards thus fitted up, 106 infants were treated during the course of a number of months; of these fifty-two were suffering with respiratory infections on entrance. In the two wards there were but two new infections, showing a tremendous reduction in comparison with the number of new infections in the other wards. Twenty cases of whooping-cough and five cases of measles were also treated with no secondary infections; varicella was, however, conveyed five times, confirming the experience of Lesage. The box system also showed itself incapable of preventing the spread of diphtheria bacilli from carriers; these were transmitted fifteen times. Cases of clinical diphtheria were few. The nutritional results were extremely good; of healthy children over 1 month, all gained well. Many children under 1 month on simple milk mixtures thrived, which Meyer believes is rare in infants' hospitals and asylums. Very good results were seen in children who in the other wards had suffered from recurrent infections with consequent disturbances in nutrition; in the boxes, where such infections were avoided, the weight showed an immediate and steady rise.

This article is extremely interesting as suggesting means for the prevention of these hospital infections. It is doubtful, however, whether the method could be used unmodified in the American summer climate.

Chapell and Brown[91] also emphasize the importance of respiratory infections in hospitals; they believe that the spread of contagion both by contact and by air infection should be guarded against. As a prophylaxis against infections of the respiratory passages they have tried a systematic biweekly douching of the posterior nasopharynx with a special syringe. This is so constructed that danger of forcing fluid into the eustachian tubes is avoided. They report a marked reduction in the number of infections in the wards where this douche was used, as compared with the control wards.

Triboulet[92] is so convinced of the danger to infants of the infections to which they are exposed in hospitals, that he advises the exclusion from infants' hospitals of both normal and atrophic infants. Only infants with acute disturbances should be admitted, their stay should be as short as possible, and they should be isolated in "boxes" to prevent the spread of contagion.

Langstein[90] also believes that in the course of acute infection, the digestive juices are decreased, and that there is some change in the cells so that the ability to bind water is injured. As a diet in acute infections he warns especially against one rich in carbohydrate and salt and advises one with a high percentage of proteid. Albumin milk is here indicated; if this is not obtainable, he advises a milk mixture with little sugar, and with the addition of some preparation of proteid such as nutrose or plasmon. He criticizes the administration of malt soup in pyelitis; this has been recommended on account of its high alkalinity. He believes that on account of its high percentage of sugar it is very dangerous in acute infections. Two symptoms which are especially difficult to combat in infectious diseases are vomiting and anorexia. Both of these he treats by feeding with a stomach-tube, with good results. Rosenstern[10] treats the anorexia of children with acute infections by the giving of concentrated albumin milk. This can safely be given after the third month; by this means he has succeeded in feeding children with pneumonia, cystitis and pertussis so that there was no loss but even a gain in weight during the infection.

The Influence of Heat on Nutritional Disturbances

93. Rietschel: Jahrb. f. Kinderh., 1913, lxxviii, 312.
94. Schereschewsky: Arch. Pediat., 1913, xxx, 916.
95. Wolff: Jahrb. f. Kinderh., 1913, lxxvii, 569.
96. Zahorsky: Am. Jour. Dis. Child., 1913, vi, 289.
97. Bleyer: Am. Jour. Dis. Child., 1913, vi, 319.
98. Knox: Arch. Pediat., 1913, xxx, 191.

The complicated problem of the relation of hot weather to nutritional disturbances is still a field for controversy.

Rietschel,[93] who has written so much on this subject, has given a general review of his own theory. He believes that the action of heat as a cause of summer diarrhea is a direct one (it acts, that is, by a direct injury to the child); not an indirect one through the spoiling or bacterial infection of milk. This direct action may be either an acute heat disturbance, corresponding to a heat stroke in an adult; or a chronic injury of a very complex nature, through which the reaction of the child to injuries, such as those of artificial feeding, infection, etc., is changed. This action he compares to the general lowering of nutritional function observed in cases of parenteral infection; here, too, there may be many factors, such as lowering of the amount and ferment activity of the digestive juices, a lowered tolerance to all foods, a lowered resistance to all infections, or a secondary change in the intestinal flora. The temperature of the house, he reasserts, is all-important, as this may be far higher than the outdoor temperature. Very different clinical pictures may result from the interaction of different factors with heat. Spoiled milk he rejects as an important cause of summer diarrhea, on account of observations in which infants fed on bad milk but with other conditions favorable, developed no symptoms. That spoiled or infected milk causes diarrhea, is merely a theory, and so far absolutely lacks proof, he believes. He admits that dysentery may be transmitted in this way in epidemics, but considers this rare.

Schereschewsky[94] gives an excellent review of the literature on the relation of heat to infant mortality, with a very complete bibliography. His conclusions coincide, for the most part, with those of Rietschel. He believes, however, that a certain proportion of cases of summer diarrhea is due to specific infections, in the dissemination of which contact and flies are important. He lays great stress on the importance of good housing conditions and of rational hygienic care in the protection of infants against the dangers of hot weather.

Wolff[95] reports an interesting case which bears on Rietschel's theory that heat alone, without change in the feeding, may cause a diarrhea. A premature infant, fed on albumin milk, was accidentally overheated in an incubator, in which the bottles were too hot. The child's temperature rose to 42 C. and it had bad stools. On removal from the incubator and after a cool bath, the temperature fell to normal and the diarrhea ceased; the feeding had been continued unchanged throughout.

Zahorsky[96] finds no regional variation in the summer mortality of infants in different parts of the United States, except that a few western cities show remarkably low figures. He finds a higher mortality

in manufacturing cities. He has studied the relations between the mortality and heat curves in St. Louis for several summers and concludes that there is a relation between them which is more marked in spring than in the later summer. He has observed in many cases that very hot weather produces fever in infants; but he does not believe that it produces diarrhea, and believes that the evidence is against Rietschel's theory that the direct action of heat may cause diarrhea. In a foundlings' home under his care the summer mortality has greatly diminished since proper pasteurization and refrigeration of the milk has been instituted. He concludes that one of the chief causes of summer diarrhea is to be sought in the organisms whose virulence and activity may be increased. Bleyer[97] found no relation between humidity and infant mortality in the course of three summers in St. Louis. He has studied especially the relation between the "heat peaks" and the "mortality peaks" and finds a correspondence in only 22 per cent. of cases.

Knox[98] ascribes chief importance in the prevention of summer diarrhea to breast-feeding, feeding with pasteurized milk, and to sensible care of the infant.

The trend of opinion is, then, in regard to the summer hygiene of infants, to lay stress not only on the administration of milk of low bacterial count, but also on all measures to prevent overheating, such as very light clothing, frequent baths, and free circulation of air in houses.

NOTES ON ESPECIAL NUTRITIONAL DISTURBANCES

99. Hirschfeld: Jahrb. f. Kinderh., 1913, lxxviii, Erg. H., 197.
100. Bauer: Monatschr. f. Kinderh., 1913, xii, 510.
101. Hess: Am. Jour. Dis. Child., 1913, v, 298.
102. Helmholtz: Jour. Am. Med. Assn., 1913, lxi, 2188.
103. Langstein: Jahreskurs f. Aerztl. Fortbildg., 1913, iv, No. 6.
104. Frank: Jahrb. f. Kinderh., 1913, lxxvii, 163, 333, 422.
105. Monti: Wien. med. Wchnschr., 1913, lxiii, 2262.
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107. Clock: Jour. Am. Med. Assn., 1913, lxi, 164.
108. Variot, Lavialle and Rousselot: Bull. Soc. de Pédiat., 1913, xv, 337.
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110. Rosenhaupt: Deutsch. Med. Wchnschr., 1913, xxxix, 752.
111. McClure: Am. Jour. Dis. Child., 1913, vii, 48.
112. Huldschinsky: Ztschr. f. Kinderh., 1913, viii, 363.
113. Aschenheim: Ztschr. f. Kinderh., 1913, viii, 161.
114. Brünig: Arch. f. Kinderh., 1913, lx, 116.
115. Abt: Jour. Am. Med. Assn., 1913, lxi, 1275.
116. Grulee: Interstate Med. Jour., 1913, xx, 41.

Alimentary Intoxication

In intoxication the relation of the symptoms to those of disturbances of the vegetative nervous system has been studied.

Hirschfeld[99] has used Loewi's test in many cases of intoxication. In the normal individual one drop of one per mille epinephrin solution in the conjunctival sac will cause no mydriasis; in cases showing increase in the tonus of the sympathetic system a dilatation ensues. In ten cases of alimentary intoxication the test was positive. Among the 255 other cases examined, no condition gave the sign with any constancy. She concludes that an increase in the tonus of the sympathetic system is characteristic of alimentary intoxication.

Bauer[100] describes a distention of the lung observed in three cases of severe intoxication in infants, in two of which clinical diagnosis of the condition was proved at necropsy. He believes that this is fairly constant in intoxication, and that it predisposes to pneumonia. He draws attention to the resemblance of this condition to the distention of the lung seen in asthma and in animals after anaphylactic shock and peptone poisoning.

Hess[101] has studied the pancreatic secretion of ten infants with acute intoxication, comparing it with that of three control cases with high fever. Material for examination he obtained by means of his duodenal catheter. He found a deficiency of lipase in the cases of intoxication, with a normal secretion of amylase and trypsin; these conditions were not present in the control cases. In cases of atrophy with a total increase in the amount of secretion he also found a diminution in lipase.

Helmholtz[102] in cases of intoxication has used subcutaneous injections of 50 to 200 c.c. daily of a 6 per cent. solution of dextrose in Ringer's solution, on the principle that the dextrose can be used directly as a food. Among the twenty cases reported, not one showed sugar in the urine. Edema was seen rarely. The dietetic treatment was the usual one: tea or water for twelve to twenty-four hours, followed by small quantities of breast milk or albumin milk, which were gradually increased. The patients in the cases reported were, for the most part, in very poor condition on entrance. Advantages seen from the use of the solution were: improvement in the turgor of the skin, in the circulation, and in the mental condition, the coma disappearing more rapidly on this treatment.

Feer[47] believes that in intoxication albumin milk is sometimes even preferable to breast milk.

Ileocolitis

It has been shown that the etiology of ileocolitis, or "diarrhea from infectious origin" has been the subject of a great deal of study. As to the treatment there have also been many publications. The treatment advised by Kendall[80] and his coworkers has already been reviewed.

Most German writers believe that in this type of diarrhea alone albumin milk is ineffectual. Benfey (as above) states that Finkelstein, here also, has achieved good results with the food. Langstein[103] believes that no great advance has been made in the treatment of this condition. He has used albumin milk, also the buttermilk treatment recommended by Schaps, without success.

Frank[104] reports a series of seventy cases of "dysentery-like" diarrhea treated with whey. The cases showed, for the most part, blood and pus in the stools, and were, she believes, of an infectious origin in children already suffering from acute and chronic nutritional disturbances. She recommends the use of a combination of whey with cereal water. This food contains a high percentage of salt and very little carbohydrate; it is easily tolerated and marked losses in weight are prevented by the high salt content. She acknowledges that the treatment seems contradictory to the beliefs at present in force as to the damage caused by a high whey concentration; Feer's[58] observation, however, of its harmlessness in the absence of sugar and fat, and Langstein's of the same nature, would seem to explain this point. She warns against prolonged starvation in cases which have been fed on a diet rich in carbohydrates. In early cases she advises castor oil and rectal irrigation, with hunger for twenty-four hours, followed on the second day by five feedings of 50 gm. each whey and cereal water, increased on the third day. In mild cases milk may be added in small amounts at this time and gradually increased; in severe cases not till the fifth to eighth day. She warns against tannigen and tannismuth as they frequently induce vomiting, but gives bismuth subnitrate from the sixth to twelfth day. Full histories of the seventy cases are appended.

Monti[105] advises tannismuth in dysentery and infectious diarrhea.

Grulee[116] has used a purely proteid diet in these cases with good effect; this consists of the curd of skimmed milk suspended in a 5 per cent. gelatin solution. Previously he used an arrowroot water as a diluent. This diet cannot be continued more than four days to a week. The gelatin water is gradually replaced by buttermilk, and the skimmed milk curds by those from whole milk, the diet then being albumin milk. He uses no drug except occasionally small doses of paregoric. He does not speak of any symptoms of sugar starvation arising on this diet; on theoretical grounds one would expect them.

Mehl-Nährschaden

The symptom complex known by this name has been described again at some length by Langstein.[8] It is caused by an exclusive diet, long continued, of carbohydrates, and is marked by a hypertonic condition of the muscles, atrophy, and in one type of cases by edema.

Abt[115] reviews the literature on this condition, and reports two cases of his own.

Frank and Stolte[106] have made chemical analyses of the liver in cases of this disturbance, and have found a decrease in dry substance and an increase in water as compared with analyses of the liver of control cases. They conclude that the disturbance leads to an increase in water throughout all the tissues, which explains the clinical fact of the very low resistance of these children to infection.

Lactic Acid Bacilli

Clock[107] reports the treatment of 117 cases of all forms of diarrhea with cultures of *B. lactis bulgaricus*. One or two tablets every two or three hours were given in mild cases; in severe ones two or three tablets at the same intervals. The diet varied; in most cases, the previous diet was continued; in some, starvation, followed with small amounts of boiled milk. Good results were shown by gain in weight and a rapid change in the nature of the stools. That this treatment should be successful in all forms alike of nutritional disturbance seems strikingly at variance with all theories in regard to their etiology. Kendall[80] has shown that in a certain group of infectious diarrheas, those caused by the gas bacillus, the administration of lactic acid bacilli is indicated. Further study and confirmation of Clock's results must be awaited.

Vomiting and Rumination

Variot, Lavialle and Rousselot[108] again recommend the administration of condensed milk with a very high percentage of sugar in cases of continued vomiting in infants. They ascribe its good effects to a change in the casein, making it resemble more closely that of breast milk.

Sébilleau[109] advises the administration in these cases of a tablespoonful of a 1.7 per cent. solution of sodium citrate before each feeding.

In nervous vomiting Rosenhaupt[110] recommends anesthetizing the mucous membrane of the stomach. As cocain is too poisonous he advises the use of anaesthesin.

McClure[111] reports a case where nervous vomiting had reduced an infant to a state of extreme atrophy. Vomiting ceased at once when the child was given a semi-solid diet of one part farina, with six parts of whole milk; recovery ensued.

Rumination associated with uncontrollable vomiting was also successfully treated by Huldschinsky[112] with a similar semi-solid gruel.

Cases of rumination have been reported by Aschenheim[113] and by Brünig.[114]

The Influence of Other Factors on Nutrition

117. Birk: Monatschr. f. Kinderh., 1913, xii, 1.
118. Miller: Arch. Pediat., 1913, xxx, 538.

The influence of psychic factors on the nutritional condition of infants has been suggested as a possibility by Czerny. An unfavorable psychic condition has been suggested as one factor in the condition of hospitalism. Birk[117] reports two cases in proof of this theory. He believes that psychic stimulation and happiness are necessary for the nutritional well-being of the infant.

Theories as to the influence of teething are reviewed by Miller.[118] The older writers ascribed many morbid symptoms to teething, while the modern tendency is to deny any connection between them. Miller takes a middle position, believing that in teething there is a reflex hypersensitiveness of the intestinal tract.

Anorexia

119. Tobler: Deutsch. med. Wchnschr., 1914, xl, 313.

The importance of anorexia as a symptom most often seen in disturbances secondary to parenteral infections, and also in young infants on the breast, and its treatment, as discussed by Langstein and Rosenstern, has already been reviewed. Rosenstern[10] says that young infants on the bottle sometimes fail to take enough because the food is so much diluted that they cannot drink enough at one feeding if five feedings daily are given. He advises a temporary increase in the number of feedings to eight until the concentration of the food can be increased; then a return to five or six feedings may be made. He considers as another important factor in apparent anorexia, the marked air-swallowing shown by some infants. They stop sucking merely because the stomach feels too full. If such children are raised to a sitting position once or twice during feeding and are allowed to eructate swallowed air, they will afterward take more nourishment.

Tobler[119] gives many practical points as to the treatment of anorexia; some of them are those already given above. He has seen little effect from radix gentianae lutae, which may be administered, as 3 to 6 drops of the "dialysat golaz" in sweetened water a quarter of an hour before feedings. Pepsin in the form of pepsin Grübler, 3 to 5 minims, ten minutes before feedings in combination with small quantities of dilute hydrochloric acid sometimes is effectual; theoretically its use seems irrational. One to 3 drams of Carlsbad or Vichy water ten minutes before meals has also been used. Feeding by gavage in young infants may tide over a dangerous period; in older infants it may be useful for its psychic effect and lead to an increased taking of food.

STERILIZATION OF MILK

120. Bradley: Arch. Pediat., 1913, xxx, 579.
121. Schlossman: Arch. f. Kinderh., 1913, lx-lxi, 676.
122. Grimmer: Monatschr. f. Kinderh., 1913, xii, 657.
123. Grimmer: Monatschr. f. Kinderh., 1913, xii, 1.

Opinions are still divided as to the importance to the infant of bacterial infection of milk. In the foregoing pages many opposing views have already been cited on this subject: Rietschel,[93] Bahrdt,[24] Zahorsky,[96] etc.

In accordance with the prevailing theories of the etiology of the nutritional disturbances, many German pediatricians minimize the importance to the child of bacterial contamination of milk, while those in America, for the most part, consider it of extreme importance.

Bradley[120] expresses the latter theory in an article on milk-poisoning. He believes that pasteurization is the best method of sterilization; and advises the process in which the temperature is held at 145 F. for thirty to forty-five minutes. Pasteurization may be easily carried out in the home by the following method: Five quarts of boiling water are set aside for ten minutes; then the milk bottles are set in the water and allowed to remain for forty-five minutes. He believes that milk obtained under proper precautions should not contain more than 10,000 bacteria per cubic centimeter.

Bahrdt[24] uses centrifuging as a means of purifying milk; he finds that the pathogenic bacteria can be removed in this way. Cream can not, however, be effectually purified in this manner, nor can milk during the hot months.

Grimmer[122, 123] gives an extremely complete review of the literature for the past year on all subjects related to milk.

Schlossman[121] writes of successful experiments with Lobeck's method of preparing milk free from bacteria.

BOILED MILK

124. Lane-Claypon: Ergebn. d. inn. Med. u. Kinderh., 1913, 635.
125. Coit: Arch. Pediat., 1913, xxx, 122.
126. Morse: Boston Med. and Surg. Jour., 1913, clxviii, 726.

Lane-Claypon has made an extensive investigation under the British Local Government Board on the effects of heated and superheated milk on the infant's nutrition. This includes the report of animal experiments, made by different investigators; a report of clinical observations by various authorities on the effect of raw and boiled milk in hospitals; and a careful clinical dispensary investigation in which a series of normal breast-fed children was compared with one of normal children on boiled milk. The conclusions which she draws are these:

1. Additional proof is given that animals and infants develop better on milk of their own species.

2. Development of animals and infants on milk of their own species shows no difference whether the milk is raw or boiled.

3. On milk of a foreign species animals and infants develop slightly better if the milk is boiled.

4. It has by no means been proved that infants develop scurvy from boiled milk alone.

Coit[125] reviews the work of Lane-Claypon and emphasizes its importance.

Morse[126, 63] reviews the literature on boiled milk for the past year, also that on different methods of pasteurization of milk.

ROENTGEN RAY

127. Ladd: Am. Jour. Dis. Child., 1913, v, 345.
128. Ladd: Arch. Pediat., 1913, xxx, 740.
129. Pisek and Lewald: Am. Jour. Dis. Child., 1913, vi, 232.
130. Major: Ztschr. f. Kinderh., 1913, viii, 343.
131. De Buys: Am. Jour. Dis. Child., 1913, vi, 334.

Much work has been done on the Roentgen-ray examination of the infant stomach in normal cases and in those showing nutritional disturbances.

Pisek and Lewald[129] took series of Roentgen-ray pictures of the stomach of normal infants after a bismuth meal at intervals of ten minutes. They found no constant shape for the stomach; the shape apparently does not depend on the amount or character of the food taken, but on the amount of gas. They saw normally a rapid passage of food from the pylorus; in many cases food entered the duodenum one minute after its entrance into the stomach. They found that alkalies exercise a retarding influence on gastric motility; and that food, entering the stomach at different times, does not tend to mix.

Ladd[127, 128] has written of gastric motility in the infant as studied by the Roentgen ray. He studied fourteen infants; to these he gave 2 drams of bismuth subcarbonate in their feeding. He finds, as do the other writers, an absence of peristalsis in the infant stomach; that some food passes into the duodenum immediately after the feeding is completed, and that the stomach is emptied of the larger amount in one and a half to two and a half hours. A considerable residue then remains for four and a half to seven and a half hours. The bismuth itself does not apparently affect the motility. The effect of different elements of food is studied, but no conclusions are drawn. A large amount of proteid seems to delay the emptying of the stomach, while a moderate amount of fat hastens it.

Major[130] used barium sulphate instead of bismuth. He believes that information regarding gastric motility cannot be gained when the former substance is used, for it adheres to the walls of the stomach, and gives it the appearance of being full, when in reality there is but a thin layer of barium over the mucous membrane. (He does not say whether the same criticism must be made of studies with bismuth.) His observations as to the normal shape of the stomach agree with those of the other authors. With the infant in a sitting posture he finds the most usual shape that of an inverted retort; in a recumbent position, that of an irregular sack. The gas bubble lies usually in the pyloric region, and is due, he believes, to swallowed air. The respiratory movements of the infant influence greatly the shape and position. Peristalsis is not so marked as in the adult. He too has seen food entering the duodenum immediately after the feeding. The time of complete emptying of the stomach, when no barium is used, is one and a half to two hours. He studied the stomach also in children with nutritional disturbances; in many cases of dyspepsia and in two cases of decomposition. He saw at times a delay in emptying, at times an increase in rate.

De Buys[131] shows that the Roentgen ray may aid the diagnosis between spasm and stenosis in pyloric obstruction. In both, peristaltic waves may be seen. In spasm the stomach may lie in the normal position, and the food is slower to leave the stomach than in the normal case; in stenosis the stomach frequently lies to the left side, and the food leaves the stomach very slowly or not at all. Ladd,[127] in cases of pyloric stenosis saw peristalsis and a marked dilatation.

PYLORIC OBSTRUCTION

132. Koplik: New York Med. Jour., 1913, xcvii, 57.
133. Hess: Deutsch. med. Wchnschr., 1913, xxxix, 412.
134. Hess: Am. Jour. Dis. Child., 1913, v, 268.
135. Hess: Post Graduate, 1913, xxviii, 556.
136. Hess: Ztschr. f. Kinderh., 1913, ix, 19.
137. Putzig: Therap. Monatschr., 1913, xxvii, 25.
138. Richter: Jour. Am. Med. Assn., 1914, lxii, 353.
139. Keefe: Am. Jour. Obstetr., 1913, lxvii, 383.
140. Ibrahim: Jahrb. f. Kinderh., 1913, lxxvii, 199.
141. Strauch: Med. Rec., New York, 1913, lxxxiv, 386.
142. Ramstedt: Ztschr. f. Chirurg., 1912.

The writings on this subject have this year been extremely numerous; many, however, are merely reports of cases.

Koplik distinguishes three groups in cases of obstruction:

1. Pure spasm without a palpable tumor mass, but with explosive vomiting, visible peristalsis and a marked loss in weight.

2. Pylorospasm accompanied by a relative stenosis.

3. Typical hypertrophic stenosis.

He reports ten cases which healed without operative treatment; he makes the observation that peristaltic waves may be observed for a long time during convalescence. He says that the duodenal catheter of Hess may be useful but cannot always be introduced.

Hess[133, 134, 135] has written several articles on the use of his duodenal catheter in the treatment and diagnosis of pyloric obstruction. He has also used the tube to obtain duodenal contents for examination of the digestive ferments in normal and abnormal children and for bacteriological examination, and in the study of the cases of congenital obstruction of the bile ducts.

Putzig[137] reports favorably on a case treated with the duodenal catheter, and gives data as to the technic to be used.

As to the operative treatment, much has been written. Richter[138] reports 22 cases of pyloric obstruction in which operation was performed, with a mortality of 13 per cent. In nineteen of these cases the obstruction was due to stenosis, in three to spasm. A tumor mass was palpated in all but one of these cases previous to operation. In nineteen the operation was a posterior gastro-enterostomy. He believes that in the diagnosis, the Roentgen ray cannot be entirely relied on, as bismuth will pass through the opening even in stenosis.

Keefe[139] reports cases treated surgically; Ibrahim,[140] Strauch[141] and many others, cases recovering on medical treatment.

The operation of Ramstedt[136, 142] has been much discussed, but the posterior gastro-enterostomy continues to be the most popular in America.

DUODENAL ULCERS

143. Holt: Am. Jour. Dis. Child., 1913, vi, 381.
144. Schmidt: Berl. klin. Wchnschr., 1913, l, 593.

The reports of ninety-one cases of duodenal ulcers in infancy has been reviewed by Holt, who adds four cases of his own. From these he concludes that in the etiology atrophy is the most important predisposing cause. Seventy per cent. of the cases occurred between 6 weeks and 5 months. The ulcers were nearly all situated above the papilla, and showed macroscopically a punched-out appearance; microscopically, an absence of round-cell infiltration. As to the symptoms, in one-third of the cases there were none attributable to the ulcer. Hemorrhage was the only definite symptom; blood in the stools of an atrophic child in the absence of a diarrhea should suggest an ulcer, Holt believes. Collapse, with a concealed hemorrhage, occurred in a certain number of cases. As to diagnosis, he recommends the passage of a duodenal catheter. In one case of his own the presence of blood

in the eye of the tube established the diagnosis. He believes that the danger from this procedure is slight.

Schmidt[144] believes that duodenal ulcer is more common in infancy than has been thought. He found it post mortem in 18 per cent. of a very large number of necropsies on infants. He believes that not only atrophy but all general wasting diseases predispose to ulcer.

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REVIEW OF SYPHILIS WITH ESPECIAL RELATION TO HEREDITARY SYPHILIS*

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Part Two — Newer Therapy

The foundation on which the newer therapy of syphilis rests is composed, in largest part, of material derived from the results of the serum tests which we have just been considering in Part One. It follows that, as the solidarity of a structure is affected by the strength or weakness of its foundations, so must the opinions expressed in Part Two for and against salvarsan and neosalvarsan be judged in accordance with the estimates formed of the strength or weakness of the serum tests.

CRITICISMS

Having seen that criticism of the serum test method exists, it cannot occasion surprise that the newer therapy of syphilis should also be criticized. Klotz[67] is most outspoken in his objection to an employment of salvarsan or neosalvarsan as a routine method of treatment of syphilis. He admits that, occasionally, the newer remedies do possess a certain value, but, speaking generally, the indications for their use will be reduced to a minimum if mercury and iodids are prescribed with proper judgment and administered with thoroughness. Gaucher[47] uses the Ehrlich remedies as a last resort, i. e., when mercury has failed. He considers them both untrustworthy and dangerous. Hoffman[59] states that, if we may judge the efficiency of the newer therapy by its success in protecting the offspring of syphilitic unions, we are not yet justified in abandoning the ancient rule of forbidding syphilitics to marry until they have been under observation for at least three years. The most that we are permitted to hope from the new remedies is that we shall be able to substitute two or three injections of salvarsan for five or six courses of mercury. Experience leads Levy-Bing and Duroeux[73] to write that they cannot recommend the new remedies as the best method of treatment in hereditary syphilis. Müller[90] is in doubt as to which method is superior, mercury or salvarsan. Langford[70] favors mercury when there is visceral involvement. Noeggarath[94] considers mercury

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*This is a continuation of the abstract article appearing in April. The references will be found at the end of the first article.

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superior to salvarsan if the infant's physical condition is not good, or if a septic process exists, even one not syphilitic. Watrazewski[130] much prefers mercury to salvarsan. Shields[108] was so disappointed with the results of salvarsan that he doubts if it can either abort or cure. Nichols and Mutot[92] call salvarsan a useful adjunct to mercury. Wilson[134] opposes the routine employment of salvarsan and neosalvarsan. The present popularity he ascribes to a lamentable international hysteria, the result of "an over-riding of science by commercialism." He warns the profession that unless it takes a saner view of the uses and limitations of the new remedies, five or ten years hence every child born of syphilitic parents will inherit the disease.

De Aja replies that the criticisms prove only that the critic lacks the courage to use the remedies as they should be used. If he would only give them in adequate doses, his opposition would disappear at once. De Azua,[6] Dreyfus[33, 34] and Iverson[57] agree with de Aja that such insufficient dosage cannot be expected to give proper results. Spiethoff[113] even declares that if the total dosage is too small, salvarsan is dangerous, but that the same reproach cannot be made if adequately large. Whitehouse and Clark[133] are so enthusiastic over salvarsan therapy that they assert that a disease which salvarsan does not at least relieve cannot be syphilis.

METHODS

Almkvist[5] says that, in his opinion, a combination of salvarsan and mercury is the best method of treatment. He reasons that the cure of syphilis is produced by the continuous action of substances on the spirochetes. Salvarsan cannot exert such an effect for, acting in the blood-stream, it does not reach the spirochetes hidden in the tissues. Mercury used alone cannot cure for the reason that it is impossible to give it in sufficiently large amounts without doing damage to the patient. Therefore, the only logical method is to reinforce the action of salvarsan by the supplemental effect of mercury. Barduzzi[10] says that, without mercury, salvarsan is powerless to cure. According to de Azua,[6] frequent injections are necessary if salvarsan is not supplemented by mercury. Corbus[27] believes that it is possible to cure with either salvarsan or mercury alone, but a quicker result is obtained if they are used in combination. Fordyce,[42] Mortimer[87] and Morton[89] advocate the combined method, the last because he doubts the effectiveness of salvarsan therapy. Nicholas and Mutot[92] always give salvarsan in combination with mercury. Eisenstaedt[35] and de Favento[38] get better results when the drugs are used together. Gougerot and Parent[49] say that it is immaterial which of several approved methods is chosen

provided the scheme of treatment adopted includes daily injections of some soluble mercurial salt.

Dreyfus[33] concluded that salvarsan is most effective when a total of 5 or 6 gm. is injected within six or eight weeks and followed by a course of mercurial inunctions.

Gardner[46] quotes Schreiber as advocating the administration of a total amount of 6 gm. divided into four doses and one dose injected every other day. It is to be noticed, however, that, in a more recent paper Schreiber[110] advises the very different procedure of an initial dose not to exceed 0.3-0.4 gm., and, instead of every other day, subsequent injections once in two weeks. Schreiber explains his changed attitude on the ground that he has come to the conclusion that the customary dose in Germany is too large and that the too frequent repetition predisposes to undesirable cumulative action. Iverson,[60] following Schreiber's earlier method, gives one injection every other day up to the number of four. Four, McDonagh[82] thinks, is the smallest number of salvarsan injections which is likely to cure. Lueders[76] reports that, to relieve deafness, he had to give six injections of salvarsan in the course of ten weeks in order to secure the result.

Gardner[46] found 1.5 gm. in 20 c.c. water a satisfactory dose of neosalvarsan. McIntosh and Parker[84] injected 0.6 gm. in a solution of 150 c.c. of bacteria-free distilled water. In the primary stage they give two initial doses, with a third after three weeks. In the secondary stage, they first inject three doses and, after an interval of eight weeks, a fourth. Tertiaries they treat by an injection every two or three months until the W. R. becomes negative. Stühmer[118] advises doses of neosalvarsan of not over 0.4-0.6, repeated at intervals of ten days.

Scholtz and Riebes[109] have adopted as a routine method two successive injections of 0.4-0.5 gm. of salvarsan within twenty-four hours, followed by daily inunctions of mercury for three or four weeks together with a subcutaneous injection of mercury once every five to eight days. Then, they repeat the series for a second time. They report that, by using this method, they have had but one accident in 1,200 cases and neurorecurrences have been eliminated. They also report that they have recently given three successive injections of 0.4-0.5 gm. of salvarsan within a period of twenty-four hours with no untoward result. Marshalko and Veszpremi[80] do not think such large amounts of salvarsan are necessary, as smaller doses are just as effective and likewise safer. It is interesting to read in this connection that Szametz[121] obtained a brilliant result in a case of chorea from a dose of only 0.2 gm. of salvarsan. Wechselmann[131] urges giving smaller doses of salvarsan than is customary at the present time. Spiethoff,[113] on the other hand, states that if salvarsan is to be used at all, at least

in secondary syphilis, the dose should certainly not be small. He would follow salvarsan with mercury in order to prevent recurrence.

Müller[99] states that intramuscular injections of salvarsan produce more lasting effects than intravenous.

Gruenberg[52] prefers salvarsan to neosalvarsan when it is desired to try to abort the disease, to treat secondary cases, to give large doses or frequent injections or to obtain a rapid effect. Whitehouse and Clark,[133] from one or more inpections of salvarsan, obtain the same effects as with four or more injections of neosalvarsan.

The newer remedies do not protect the offspring from his syphilitic parents much more effectually than the older (Hoffman[59]). The children of the next five or ten years will be subjects of inherited syphilis if the present blind confidence in salvarsan and neosalvarsan continues (Wilson[134]). Experience does not commend the Ehrlich remedies as the best treatment for inherited syphilis (Levy-Bing and Duroeux[73]). It is a question whether the newer therapy is more efficient than the older (Müller[90]). The administration of salvarsan was followed by death in two cases of hereditary syphilis (King-Smith[66]). Salvarsan is more dangerous in the presence of visceral, inherited syphilis (Langford[70]). While Ehrlich's warning that salvarsan should not be used in infants has received little support in fact, nevertheless, it is true that poor physical condition and septic disease of any origin constitute contraindications to its employment (Noeggarath[94]). Salvarsan should never be used under any condition for the deafness of hereditary syphilis (Beck[11]). Salvarsan may be used in such cases, but, probably, better after mercury (Voorhees[127]). Only the future can prove that large doses of salvarsan in concentrated solutions are really as harmless as they seem and alone can teach us in which forms of the inherited disease salvarsan is not to be used (Noeggarath[94]). Although he obtained the result in two of his nine cases, Welde[138] is impressed by the obstinate resistance which the positive serum reaction of hereditary syphilis offers to the injections.

Opinions differ as to the value of the new remedies in the special manifestations of inherited syphilis. In interstitial keratitis, general opinion is not favorable to them. Post[101] reports that his results were good. In the hereditary syphilis of bones, skin and mucous membranes, Langford[70] found salvarsan, as a rule, less efficient than mercury. In the exceptional cases, resistant to mercury, salvarsan was more efficient. Steiger[114] was well pleased with salvarsan in hereditary syphilis when given intramuscularly in the form of a 40 per cent. suspension in iodopin. Swift and Ellis[119] were impressed by the results from the administration of the milk of salvarsanized mothers to nurslings. On the other hand, King-Smith[66] was unfavorably impressed.

HEREDITARY SYPHILIS AND DOSAGE

The literature contains very little concerning the most effective dose of the newer remedies in the treatment of inherited syphilis. Noeggarath[94] estimates that, in syphilis of children, the initial dose should correspond to 0.0002 gm. salvarsan per each kilo of body weight. Succeeding doses should be gradually increased in amount until they reach 0.1 gm. per kilo of body weight. King-Smith[66] likewise advises beginning with small doses and increasing the size gradually. Compared to adults, children bear relatively large doses of salvarsan (King-Smith[66]) and of mercury if the liver and kidneys functionate perfectly (Levy-Bing and Duroeux[73]).

Ordinarily, salvarsan is, as in adults, injected intravenously. The choice of a vein for the operation differs with the preference of the individual operator. Some use the veins of the head. King-Smith[66] prefers the jugular vein. Weil, Morel and Moriquand[132] tried, experimentally, rectal injections. Somewhat to their surprise, they found that children bore rectal injections well if a little laudanum was added to the salvarsan solution. The disappearance of the visible signs of the disease proved that, contrary to the experience in adults, the drug was, in children, actually absorbed from the rectum. Neither local nor systemic reactions occurred.

ACTION OF SALVARSAN AS SHOWN BY THE URINE

Hitherto, we have considered the action and effect of salvarsan and neosalvarsan only from the clinician's point of view. There have been published, however, reports showing that attempts have been made to secure evidence from other sources. Capelli[21] thinks that his investigations of the nitrogen excretion by the kidneys demonstrates that salvarsan is a disturber of metabolic processes. Capelli found the nitrogen output was increased (2 gm.) for twenty-four hours after an intravenous injection of salvarsan notwithstanding a decrease in the nitrogen intake of 6 gm. After twenty-four hours, the nitrogen excretion fell to 1.8 gm. below the ingestion. The excretion urea was perceptibly reduced. Capelli attributes the primary increase to a "Herxheimer reaction" and the presence of a slight fever. His final conclusion is that salvarsan alters the metabolism in syphilitic subjects, producing a temporary increase and a subsequent, more lasting decrease in the excretion of nitrogen. Greven,[51] using a so-called "biological method," reported that salvarsan could be detected in the urine within an hour after its injection. He found evidence of its continued presence for fourteen days after subcutaneous injections and for seventeen to eighteen days after intramuscular. He thought that mercury hin-

dered excretion while the iodids favored. Lorenz[75] found arsenic in the urine one-half hour after an intravenous injection of salvarsan. Twenty-eight to fifty-seven hours later he could discover only a slight trace.

SALVARSAN IN THE BLOOD

Scholtz and Riebes[109] failed to discover a trace of salvarsan in the blood-serum four to six hours after the injection.

SALVARSAN AND THE CEREBROSPINAL FLUID

Lorenz[75] found that the lymphocytosis and increased globulin content in the cerebrospinal fluid was reduced by salvarsan. Levy-Bing, Duroeux and Dogny[71] report that there occurs, after salvarsan, a true hypertension of the cerebrospinal fluid which is always accompanied by an increase in the amount of albumen. They do not doubt that salvarsan causes meningeal reactions more frequently than mercury.

SALVARSAN AND BLOOD-PRESSURE

In twelve cases of mental disease, McKinnes[83] could not demonstrate that salvarsan increased the blood-pressure even when given in so large a volume as 195 c.c. of the solution.

LETHAL DOSE

Merian, Girauld and Duret[85] endeavored to determine the fatal dose of the two substances in rabbits. The lethal level of neosalvarsan was approximately in the proportion of 0.42 gm. per kilo body weight. The toxic dose varied from 0.14 gm. upward. With salvarsan, the lethal level was reached at 0.10 gm. per kilo body weight.

CAUSE OF THE SALVARSAN REACTIONS

Marshalko and Veszpremi[80] do not believe that the so-called "water-error" plays any part in the production of the systemic symptoms of reaction after salvarsan. Nobl and Peller[93] could not demonstrate the bacterial contamination of the solution to be a cause of the fever. They doubted also if the fever after salvarsan was due to circulating endotoxins. They concluded that the more recent the generalization of the systemic symptoms of syphilis and the larger the relative dose of salvarsan, the greater was the febrile reaction. Wachenfield[129] considers it still remains to be proved that salvarsan reactions are due either to the solvent, to bacteria or to bacterial toxins.

Schreiber[110] suggests that the untoward symptoms which occur after injections of salvarsan and neosalvarsan may be due to a species of anaphylaxis. Plausibility is lent to the idea by Swift's success in

reproducing the symptoms of anaphylaxis in guinea-pigs by means of repeated injections of salvarsan. In this connection it is not to be forgotten that Gradwohl's[50] explanation of the luetin reaction was that it was a phenomenon of anaphylaxis. Stühmer[118] ascribes the salvarsan reactions to "auto-anaphylaxis," a state especially favored by certain conditions such as, for example, the increased susceptibility of the auto-intoxication of pregnancy.

De Aja[1] has observed that immediate and late reactions after salvarsan injections occur more frequently in cases in the secondary stage of syphilis. De Azua[6] agrees that the secondary stage favors relapse. Nicholas and Mutot[92] and Gruenberg[52] have seen neurorecurrences develop in cases of secondary syphilis in spite of energetic treatment. Rimini[107] is convinced that the secondary cases offer a peculiarly stubborn resistance to curative treatment.

It is an accepted fact that the secondary stage of syphilis yields the greatest percentage of positive results to the serum test. The writers just quoted assert that the greatest frequency of neurorecurrences is in secondary syphilis. The question is unavoidable, What is the connection between these facts?

DEATHS AFTER SALVARSAN

Several fatal cases have been reported during the past year, one by de Favento,[38] one by Keyes,[65] three by Hirsh[57] (of which one case was his own and two Hammer's), two of hereditary syphilis by King-Smith,[66] one by Newmark[91] and one by Marshalko and Veszpremi.[80]

The number of salvarsan injections is in the thousands. The fatalities can almost be reckoned in single figures. Nevertheless, it is not disputed that a certain small number of patients have died under circumstances which threw suspicion on the injected remedy as the cause. The partisans of salvarsan maintain that the remedial substance should not be held responsible, but preexisting forces with which it has no connection except in so far as it may have acted as the exciting agent which stimulated these forces into fatal activity. The opponents declare that the direct cause of death is the toxic action of salvarsan. To the ordinary reader the conclusion would seemingly be unavoidable that occasionally salvarsan is the cause of death, perhaps directly, perhaps indirectly.

AUTOPSY EVIDENCE

Marshalko and Veszpremi[80] concluded that, in their case, changes found at the autopsy pointed to the fact that the fatal encephalitis was caused by the toxin action of the salvarsan. They could find no actual signs of inflammation, but only multiple hemorrhages into the brain from stasis or thrombosis without any changes of especial significance

in the substance of the brain. De Faventa[38] thinks that the bacterial contamination of the solvent was the cause of the findings in his fatal case. Newmark[91] reports the autopsy of a patient dying after an intramuscular injection of 0.3 gm. salvarsan into each buttock in which a softening of the cord was present.

NEURORECURRENCE

As ordinarily used, neurorecurrence refers to the symptoms which develop in some part of the nervous system after a considerable time has elapsed since the last treatment. The question of the comparative frequency of the condition after salvarsan and neosalvarsan and after mercury and the iodids has been sufficiently discussed above. The theories of the relationship of the action of the remedial substances to the development of the symptoms of neurorecurrence demand more attention. Some say that they are the direct result of the toxic action of the drugs. Some say that they are not the result of toxicity, but of insufficient dosage; that the symptoms are not to be attributed directly to the action of the remedies themselves, but to the latent foci of disease which they have accidentally stimulated into action.

Wechselmann[131] considers neosalvarsan more neurotropic than salvarsan, and at the same time, clinically and serologically less active. De Aja[1] thinks salvarsan is less able to prevent neurorecurrences than is mercury. Ellis[36] denies that salvarsan in any way predisposes to these nervous relapses. Fordyce[42] has never had a case of neurorecurrence in the auditory nerve after salvarsan. Gardner[46] thinks there is no choice between salvarsan and neosalvarsan so far as relapses are concerned. Gruenberg[52] considers the effects of neosalvarsan more cumulative and more toxic than of salvarsan. Kall[62] believes neosalvarsan is the more neurotropic and, in ambulants, the more dangerous. Mortimer[87] does not think it is proved that salvarsan harms the nervous system. Müller[90] reports that, in 200 salvarsan cases, 7.5 per cent. of the patients developed symptoms of neurorecurrence within seven to twelve weeks. Dreyfus[33, 34] states that neurorecurrences have become more frequent since the introduction of salvarsan. Ravaut[103] says that, in the presence of spirochetes salvarsan is neurotropic, that is, predisposes to affections of the nerves. Whereas, under ordinary conditions, without salvarsan, syphilis causes a meningeal reaction in 67 per cent. of all cases, after salvarsan medication, the figures are raised to 87 per cent. He therefore concludes that salvarsan should be used with caution if the cerebrospinal fluid shows signs of meningeal reaction. Spiethoff[113] agrees that since the introduction of salvarsan, neurorecurrences have become more frequent, not, however, because of the salvarsan, *per se*, but because of the timidity of the operator.

Schreiber,[110] once the advocate of high dosage, now believes that the massive and frequent doses customary in Germany are dangerous. Marshalko and Veszpremi,[80] from the autopsy evidence of their fatal case, conclude that salvarsan is safer in small doses. Nobl and Peller[93] say that salvarsan is toxic. Wolff and Melzer[136] concluded that neosalvarsan is more toxic than salvarsan. Gruenberg[52] thinks neosalvarsan the less toxic and its effect the less cumulative. Kall[62] belongs to the group of those who, advocating one, refer incidentally to the toxic properties of both. He advocates salvarsan on the ground that it is *less* dangerous and *less* neurotropic than neosalvarsan. Noeggarath[94] wonders what the future will show is the effect of concentrated solutions injected intravenously. Levy-Bing and Duroeux[73] say that the symptoms of toxicity are largely dependent on the functional perfection of the liver and kidneys. Rimini[107] declares that the symptoms of neurorecurrence which follow after salvarsan are due to the lighting up, by the injections, of old foci of disease. Mortimer[87] also attributes the symptoms of nervous involvement to the reawakening of a previous luetic process, possibly an accumulation in the nerve tissue of spirochetes which have escaped destruction (Müller).[90]

DOSE AND NEURORECURRENCE

De Aja[1] says that it is not the salvarsan to which neurorecurrence is due, but to the use of too small an amount to prevent the event. Almkvist[3] argues that if it were only borne in mind that it is necessary to sterilize the organism to prevent neurorecurrences, more frequent injections would be given. De Azua[6] proportions the frequency of repetition to the urgency of the case. Ravaut[103] once wrote that the likelihood of neurorecurrence went hand in hand with the frequency of the injections (the dosage). Dreyfus,[33] replying to Ravaut's later paper,[103] does not deny the accuracy of Ravaut's observations, but says that they are based on the results of a too timorous use of the remedy. Spiethoff[113] states that neurorecurrences occur in inverse ratio to the intensity of the salvarsan therapy. Iverson[60] declares that, rather than favoring neurorecurrence, high doses of salvarsan are preventative. Scholtz and Riebes[109] concur.

AUDITORY SYMPTOMS OF NEURORECURRENCE AND SALVARSAN

Rimini[107] reports eight cases of hereditary syphilis in which the auditory symptoms of neurorecurrence seemed to have been the direct result of salvarsan medication. Not one patient had ear symptoms before salvarsan. One to three months after the injections all had developed symptoms of aural disease. According to J. C. Beck,[12] the symptoms of neurorecurrence in the ear may appear at any time from

two to eight months after the salvarsan. As salvarsan may possibly predispose to the conditions, Beck thinks it inadvisable to give it to hereditary syphilitics with symptoms of aural involvement or to adults whose ear symptoms have developed within six to eight weeks of a previous injection. Biggs[13] reports a case in which deafness developed within forty-eight hours after salvarsan was injected. Carpenter[23] thinks that salvarsan is least effective in the treatment of syphilitic affections of the organs of special sense.

THE EYE

In the diagnosis of hereditary syphilis, the ocular manifestations of the disease have a peculiar importance. One result of the Ehrlich remedies has been to give us a more accurate conception of the changes which hereditary syphilis produces in the eye. Many symptoms which earlier were attributed to the deleterious effect of salvarsan medication have been shown by recent careful study to have resulted from pre-existing syphilitic processes and not from the action of the remedy.

Stiern has drawn from statistics the conclusion that only one-half of all syphilitic fetuses are born alive, and that 80 per cent. of the living half develop some form of ocular syphilis, most often an interstitial keratitis. Neumann is said to have found that 81.9 per cent. of the syphilitic infants in his clinic had symptoms of iritis. Oscar Dodd[32] estimated that, of every 5,000 cases of all forms of eye disease, one will be a manifestation of syphilis which, in 1 or 2 per cent. of the total, is some form of disease of the orbit. He says, the primary manifestation may be either an involvement of the orbital margin, a periostitis or a gumma of the orbital wall. The prognosis is worse in hereditary syphilis than in the acquired form.

The eye symptoms indicative of involvement of the central nervous system are even more serious. According to Knapp,[68] if it is desired to avoid irreparable damage, the symptoms must not escape immediate recognition. In the diagnosis of ocular syphilis, Knapp found the W. R. of inestimable value. Monradian[88] thinks its value in these cases is doubtful.

Otchaposky's results from the salvarsan treatment of ocular syphilis were disappointing, which is contrary to Post's experience. Of the 120 cases reported by Otchaposky, only forty-five showed any improvement. He even saw the other eye attacked while treatment was in progress. His best results were obtained in iritis, although, at that, the best were not so good as with mercury and the iodids. Relapses were more frequent. Reese[105] considers that salvarsan is an indispensible adjunct to mercury in the treatment of ocular syphilis without, however, being able to replace mercury.

NEURORECURRENCE; SITES OF PREDILECTION

Returning to the general subject of neurorecurrence, the fact is at once interesting and suggestive that when its symptoms develop after treatment, they seem to exhibit a distinct tendency to limitation to some one nerve trunk and that certain nerves seem to be particularly susceptible. Thus, de Aja[2] says that a very large majority of the cases of relapse affect one of three nerves which, in order of frequency, are the facial, the acoustic and the trigeminal. Fully 50 per cent., he says, occur in the facial nerve and are peculiarly obstinate to treatment compared to the ease with which other nerve systems respond.

DO SALVARSAN AND NEOSALVARSAN CURE?

A committee once met to consider how patients afflicted with syphilis might be cared for most efficiently. In the course of the discussion the question was raised as to whether a specialist in syphilis was to be preferred to a general practitioner. A physician of more than ordinary attainments rose and stated as his opinion that the care of the syphilitic to-day is not the intricate and complex problem of a few years ago which a specialist alone could handle. Then we had nothing to guide us but clinical experience. To-day, our position is different. With means of testing the blood at command, the detection of the disease is assured. By injections of salvarsan, its cure is easy.

The climax of the speech is in the last three words, "cure is easy." Whether we shall agree or disagree with the speaker, depends on our interpretation of the discussion of salvarsan and neosalvarsan in Part Two and of the serum test in Part One.

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